The Choroid Is Thicker in Angle Closure than in Open Angle and Control Eyes

Karun S. Arora,[1] *Joan L. Jefferys,*[1] *Eugenio A. Maul,*[2] *and Harry A. Quigley*[1]

Purpose. To study factors associated with choroidal thickness (CT) and to compare CT in angle closure (AC), open angle (OA), and normal eyes.

Methods. Forty controls, 106 OA, and 79 AC subjects underwent measurements of posterior CT by spectral domain-optical coherence tomography, and of intraocular pressure (IOP), blood pressure, axial length (AL), and central corneal thickness (CCT).

Results. CT was significantly greater in AC than in OA and normal eyes (HSD test, $P \leq 0.05$), but there was no significant difference between OA and normal CT; mean CT was 234, 235, and 318 μm in the normal, OA, and AC groups, respectively. With multivariable analysis among all participants, thinner CT was associated with older age, longer AL, higher IOP, and thicker CCT (all $P \leq 0.03$, $R^2 = 0.45$). Adjusting for other relevant variables, the AC group had a significantly greater CT than either the normal or the OA group ($P = 0.003$ and 0.03, respectively). In multivariable analysis including only OA and AC patients, neither cup-to-disc ratio nor visual field mean deviation were significantly associated with CT. Multivariable analysis for CT among normal eyes found longer AL to be associated with thinner CT ($P = 0.04$).

Conclusions. AC eyes had significantly thicker CT than OA and normal eyes, even after adjusting for the shorter AL in AC eyes, supporting hypotheses that choroidal expansion contributes to the development of AC disease. Age, AL, CCT, and IOP were also significantly associated with CT, while severity of glaucoma damage was not. (*Invest Ophthalmol Vis Sci.* 2012; 53:7813–7818) DOI:10.1167/iovs.12-10483

Choroidal structure and function may contribute to both normal ocular development and to the pathogenesis of ocular diseases, such as AMD, polypoidal choroidal vasculopathy, central serous chorioretinopathy, and glaucoma.[1–6] Choroidal thickness (CT) can now be measured with relative precision in vivo with spectral domain-optical coherence tomography (SD-OCT).[7,8] Factors that are associated with thinner CT in cross-sectional studies include older age, longer AL, thicker central corneal thickness (CCT), and the simultaneous effects of blood pressure (BP) and intraocular pressure (IOP), denoted by the calculated value, perfusion pressure (PP).[9–13]

The fact that CT is affected by physiological features such as BP and IOP suggests that it is a dynamic rather than a static structure. Indeed, there is known to be significant diurnal variation in CT, as well as changes in CT with a change in body position.[14–16] We recently showed that small increases in CT are induced by rapid drinking of one liter of water in persons with angle closure (AC).[17] The achievement of emmetropia depends on active mechanisms that sense image blur in the retina and signal the choroid to alter its thickness, moving the retina toward the appropriate position to reduce blur. Choroidal biochemical signals then alter scleral dimensions to maintain the axial length (AL) needed for clear imagery.[18–20] This emmetropia mechanism has been documented in chickens and mammals.[18–20] Similar changes in CT can be induced in adult humans by short-term, unilateral image blur.[21]

Prior to the development of SD-OCT, histological studies of postmortem eyes suggested that the choroid was thinner in glaucoma,[22–24] but studies of the living choroid have found no association between CT and either the presence of open angle glaucoma (OAG) or the degree of glaucomatous optic nerve damage.[9,25–28] In a previous report, we attempted to assess differences in CT among open angle (OA) patients, AC patients, and glaucoma suspects.[9] When stratified by subdiagnosis, our patient groups were too small to detect consistent differences, and we did not study normal adult eyes. The present report includes a larger group of glaucoma patients and suspects, as well as an age-matched control group to determine features associated with baseline CT, taking other known variables into account.

Methods

Subject Recruitment

Participants were selected as a convenience sample of patients and those accompanying them at the Glaucoma Center of Excellence, Wilmer Institute, Johns Hopkins. One eye of each subject was included. Subjects were >18 years old, had clear ocular media, and had no evidence of glaucoma or were diagnosed as primary AC suspects (PACS), primary AC (PAC), PAC glaucoma (PACG), primary OAG (POAG), or POAG suspects (POAGS). Diagnoses were based on criteria published by Foster et al. and applied by one of us (HQ).[29] Subjects were asked to join the study at times when a staff member was available to perform the necessary testing. Normals were included who had no prior history of eye disease other than cataract, no intraocular surgery other than cataract surgery, a healthy-looking optic nerve as

From the [1]Glaucoma Center of Excellence, Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland; and the [2]Pontificia Universidad Católica de Chile, Santiago, Chile.

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Corresponding author: Karun S. Arora, 600 North Wolfe Street, Wilmer 122, Johns Hopkins Hospital, Baltimore, MD 21287; arora.karun@gmail.com.

determined by a glaucoma specialist (HQ) with cup-to-disc ratio (CDR) <0.5, and an IOP <21. Exclusion criteria included any retinal or neuroophthalmologic disease, intraocular surgery during the previous 6 months, or secondary glaucoma. The study was approved by the Johns Hopkins Institutional Review Board, and oral consent was obtained from all subjects. The study abided by the tenets of the Declaration of Helsinki.

Study Procedures

The examination protocol was conducted in a seated position. BP measurements were obtained using an automatic blood pressure cuff (Datascope Corp., Paramus, NJ: median of 3 measurements), followed by measurement of IOP (average of 2 measurements) using a tonometer (Icare; Icare Finland Oy, Espoo, Finland). AL (median of 3 measurements); anterior chamber depth (ACD: average of 2 measurements); and keratometry (average of 2 measurements) were then measured using a biometer (IOLMaster 500; Carl Zeiss Meditec, Dublin, CA). Scans of the macular region were obtained using SD-OCT equipment (Spectralis; Heidelberg Instruments, Inc., Heidelberg, Germany).

The SD-OCT images were obtained utilizing enhanced depth imaging, which allows better visualization of the choroidal-scleral interface (CSI) than standard retinal SD-OCT images. The macular region was scanned using a single 30° linear scan centered on the fovea. Several scans were obtained, and the image with the best visualization of the border between the choroid and sclera, the CSI, was chosen.

Keratometry readings and the most recent refraction were entered into an integrated patient database software (Heidelberg Eye Explorer; Heidelberg Engineering, Heidelberg, Germany) to estimate optical magnification and, therefore, to allow for more accurate comparisons across individuals. We have previously shown that failure to correct for these variables significantly impacts thickness estimation.[9]

Image Analysis

Images were analyzed as described previously by Maul et al.[9] One choroidal image was selected for each eligible eye. All selected images, as well as the scaling factor correcting for magnification, were exported from the SD-OCT. Because the images had a fixed size, but different optical magnifications, the μm/pixel scale was different in the width dimension for each image. To analyze the images uniformly, the images were rescaled to a unified scale using image editing software (Photoshop CS5; Adobe Systems, Inc., San Jose, CA). A grid centered at the fovea and extending 3 mm (with two 1.5-mm segments) on either side was overlaid on the images. The images were then deidentified, so that the image grader was masked to the identity and diagnosis of the subject during analysis using a Java-based image processing software (ImageJ; National Institutes of Health, Bethesda, MD). The choroid was manually outlined, with the anterior border at the basal aspect of the RPE, which had a clear boundary in nearly every image. The posterior boundary, or CSI, was more variable among the images. In the majority of images, there was a hyperreflective line between the large vessel layer of the choroid and the sclera, which was marked as the CSI. When the image contained a CSI that seemed to be well delineated and thinner than the RPE, it was graded as "good." If the CSI seemed to be thicker than the RPE, the image was classified as "fair," and the CSI thickness was taken as equal to the RPE thickness (Fig. 2, Maul et al.).[9] In a few images, the CSI boundary was relatively unclear in some portion of the 6-mm zone; in these images, classified as "acceptable," the posterior choroid was marked as a smooth line joining the parts of the CSI that were clearly visible. Once the anterior and posterior boundaries were marked, the area occupied by the choroid over a 6-mm–long segment was measured and used to calculate the average CT. We have previously shown[9,17] that none of the findings are substantially different when only the "good" and "fair" images are included; hence, we included all eyes in the statistical analysis.

Data Analysis

Demographic data as well as clinical measurements were tabulated for all participants and by diagnostic group. For outcomes for which two or three repeat measurements were available (e.g., BP or AL), the median was used for analysis. The significance of differences among diagnostic groups was determined using the χ^2 test for categorical variables, analysis of variance for normally distributed variables, and the Kruskal-Wallis test for continuous variables that were not normally distributed. Pairwise comparisons among diagnostic groups were made by partitioning the χ^2 statistic for categorical variables and using Tukey's studentized range (HSD) test for continuous variables; rank statistics were analyzed in the case of continuous variables that were not normally distributed.

Univariate linear regression analysis was used to identify participant characteristics that were associated with CT. Three multivariable linear models of CT were constructed: one for all participants, one for OA and AC participants only, and one for normal participants. Independent variables for each model were chosen using the backward selection method with the criterion for staying in the model set at a probability value of 0.10. A variable included in a multivariable model was considered to be statistically significant only if the P value was 0.05 or less. Estimated coefficients and the associated variances and covariances from the multivariable model were used to make pairwise comparisons of the adjusted mean CTs for the diagnostic groups. All analyses were performed using data analysis software (SAS 9.2; SAS Institute, Cary, NC).

Results

Of 225 persons (eyes) that participated in the study; 40 were nonglaucoma controls, 106 were classified as OA (45 POAGS, 61 POAG); and 79 were classified as a form of AC (23 PACS, 30 PAC, 26 PACG; Table 1). The AC group had a significantly larger percentage of females than the other two groups. Mean CT was 34% thicker in the overall AC group than in the normal and OA groups ($P < 0.0001$, analysis of variance). Pairwise comparisons showed no significant difference in CT between the OA and normal groups, but CT was significantly greater in the AC than in the OA and normal groups (HSD test). As expected, AL and ACD were significantly shorter in AC than in OA and normal eyes (HSD test). Interestingly, diastolic PP was significantly lower in AC patients than in OA patients and normals, while mean PP was lower in the AC than in the normal group (both HSD test). The OA group had significantly larger mean CDR as well as worse average mean deviation (MD) in field testing than the AC group, likely because of the larger proportion of glaucoma patients in the OA group as compared with the AC group (58% vs. 33%).

When the subjects were split into six diagnostic groups (normal, POAGS, POAG, PACS, PAC, PACG; Table 2), the PAC and PACS groups had significantly greater CT than the normal, POAGS, and POAG groups (HSD test). Furthermore, the PAC group had a significantly greater CT than the PACG group (HSD test).

Univariate regression analysis was conducted to determine parameters related to CT (Table 3). Diagnosis was significantly associated with CT ($P < 0.0001$). While the difference in CT between normal and OA eyes was insignificant, CT in AC eyes was more than 80 μm greater than in both normal and OA eyes. Other factors significantly associated with a thinner choroid were older age, longer AL, deeper ACD, greater CDR, pseudophakia, and male sex.

Multivariable analysis including all participants selected five variables that were significantly associated with CT, with the model explaining 45% of the variance. Thinner CT was related to older age; longer AL; diagnosis (with AC subjects having a

Table 1. Characteristics of the Study Population Overall and Three Major Subgroups

	Overall		Normals		POAGS/POAG		PACS/PAC/PACG		
Characteristic	***N***	**Value**	***N***	**Value**	***N***	**Value**	***N***	**Value**	***P* Value***
CT, μm (mean [SD])	225	264 (102)	40	234 (75)	106	235 (78)	79	318 (120)	<0.0001
AL, mm (median [IQ])	221	23.6 (2.0)	37	23.8 (1.8)	105	24.2 (2.0)	79	22.6 (1.6)	<0.0001
ACD, mm (median [IQ])	218	3.15 (0.86)	39	3.36 (0.93)	101	3.30 (0.61)	78	2.77 (0.60)	<0.0001
CDR (mean [SD])	184	0.58 (0.24)	NA	—	106	0.66 (0.22)	78	0.47 (0.22)	<0.0001
DPP, mm Hg (median [IQ])	218	60.0 (13.0)	37	63.0 (14.0)	103	62.0 (13.0)	78	56.0 (12.0)	0.004
VF MD, dB (median [IQ])	184	−1.88 (4.59)	NA	—	105	−2.46 (7.05)	79	−1.15 (3.32)	0.01
Sex (*N* [%])									
Male	225	89 (40)	40	16 (40)	106	51 (48)	79	22 (28)	0.02
Female		136 (60)		24 (60)		55 (52)		57 (72)	
MPP, mm Hg (median [IQ])	218	77.0 (14.0)	37	82.0 (15.3)	103	77.8 (14.2)	78	74.4 (11.8)	0.03
DBP, mm Hg (mean [SD])	219	74.9 (10.0)	38	76.9 (9.4)	103	75.5 (10.9)	78	73.1 (8.9)	0.11
CCT, μm (mean [SD])	220	551 (39)	37	555 (33)	104	545 (41)	79	557 (38)	0.12
IOP, mm Hg (median [IQ])	222	14.5 (7.0)	37	14.0 (5.0)	106	14.5 (7.0)	79	15.0 (6.5)	0.12
Ethnicity (*N* [%])									
White non-Hispanic	225	166 (74)	40	32 (80)	106	81 (76)	79	53 (67)	0.21†
White Hispanic		2 (1)		1 (2)		0 (0)		1 (1)	
African American		42 (19)		4 (10)		20 (19)		18 (23)	
Asian		14 (6)		3 (8)		5 (5)		6 (8)	
Other		1 (0)		0 (0)		0 (0)		1 (1)	
Age, y (median [IQ])	225	67.6 (15.0)	40	65.7 (15.1)	106	67.8 (11.5)	79	68.4 (16.8)	0.87

* Significance of differences among subgroups: χ^2 test, ANOVA, or Kruskal-Wallis test.

† White versus nonwhite.

N, Number of participants in category; IQ, interquartile range; NA, not applicable/not available; DPP, diastolic perfusion pressure; VF, Visual field; MPP, mean perfusion pressure; DBP, diastolic blood pressure.

Table 2. Characteristics of the Study population, All Six Subgroups

	Normals		POAGS		POAG		PACS		PAC		PACG		
Characteristic	***N***	**Value**	***N***	**Value**	***N***	**Value**	***N***	**Value**	***N***	**Value**	***N***	**Value**	***P* Value***
CT, μm (mean [SD])	40	234 (75)	45	237 (67)	61	234 (86)	23	319 (114)	30	357 (138)	26	272 (87)	<0.0001
AL, mm (median [IQ])	37	23.8 (1.8)	45	24.3 (1.8)	60	24.2 (2.0)	23	22.1 (2.0)	30	22.5 (1.3)	26	22.8 (1.3)	<0.0001
ACD, mm (median [IQ])	39	3.36 (0.93)	42	3.42 (0.69)	59	3.19 (0.57)	23	2.74 (0.53)	30	2.76 (0.53)	25	2.84 (1.22)	<0.0001
VF MD, dB (median [IQ])	NA		45	−0.85 (2.02)	60	−4.89 (8.27)	23	−0.54 (1.88)	30	−0.59 (1.44)	26	−4.76 (10.48)	<0.0001
CCT, μm (mean [SD])	37	555 (33)	45	557 (41)	59	536 (40)	23	581 (28)	30	556 (32)	26	536 (41)	<0.0001
Previous glaucoma surgery (*N* [%])	NA		45	1 (2)	61	13 (21)	23	0 (0)	30	1 (3)	26	8 (31)	0.0002
Ethnicity (*N* [%])													
White non-Hispanic	40	32 (80)	45	37 (82)	61	44 (72)	23	17 (74)	30	26 (87)	26	10 (38)	0.002†
White-Hispanic		1 (2)		0 (0)		0 (0)		0 (0)		0 (0)		1 (4)	
African American		4 (10)		5 (11)		15 (25)		5 (22)		2 (7)		11 (42)	
Asian		3 (8)		3 (7)		2 (3)		1 (4)		2 (7)		3 (12)	
Other		0 (0)		0 (0)		0 (0)		0 (0)		0 (0)		1 (4)	
IOP, mm Hg (median [IQ])	37	14.0 (5.0)	45	16.0 (5.5)	61	13.5 (5.5)	23	16.0 (5.0)	30	15.0 (7.0)	26	14.2 (8.5)	0.01
DPP, mm Hg (median [IQ])	37	63.0 (14.0)	44	59.5 (14.2)	59	52.5 (13.0)	23	56.0 (7.5)	30	58.5 (13.5)	25	55.5 (13.0)	0.03
Sex (*N* [%])													
Male	40	16 (40)	45	19 (42)	61	32 (62)	23	6 (26)	30	7 (23)	26	9 (35)	0.08
Female		24 (60)		26 (58)		29 (48)		17 (74)		23 (77)		17 (65)	
Age, y (median [IQ])	40	65.7 (15.1)	45	66.6 (14.2)	61	68.5 (10.2)	23	66.1 (18.1)	30	63.3 (19.6)	26	71.8 (14.4)	0.11
MPP, mm Hg (median [IQ])	37	82.0 (15.3)	44	76.3 (13.5)	59	79.3 (14.5)	23	71.3 (13.0)	30	75.5 (8.2)	25	75.5 (12.7)	0.13
Pseudophakic (*N* [%])	NA		45	9 (20)	61	11 (18)	22	2 (9)	30	4 (13)	26	9 (35)	0.18

* Significance of differences among subgroups: χ^2 test, ANOVA, or Kruskal-Wallis test.

† White versus nonwhite.

Table 3. Choroidal Thickness, Univariate Analysis

Characteristic	N	CT, μm: Regression Parameter (95% CI)	P Value
Diagnosis			
Normal (*R*)	225	0	<0.0001
POAGS/POAG		1.2 (−33.4, 35.8)	
PACS/PAC/PACG		83.9 (47.7, 120.1)	
Age (per 5 y greater)	225	−12.6 (−18.3, −7.0)	<0.0001
AL (per mm greater)	221	−34.2 (−41.1, −27.2)	<0.0001
ACD (per mm greater)	218	−43.9 (−62.7, −25.2)	<0.0001
CDR (per 0.1 greater)	184	−16.2 (−22.4, −10.0)	<0.0001
Pseudophakic eye			
No (*R*)	184	0	0.002
Y		−74.6 (−112.7, −36.5)	
Sex (*R*)			
Male	225	−28.9 (−56.1, −1.6)	0.04
Female		0	
Previous glaucoma surgery			
No (*R*)	185	0	0.07
Yes		−43.5 (−89.9, 3.0)	
Ethnicity			
White (*R*)	225	0	0.65
Nonwhite		−7.2 (−38.1, 23.8)	

CI, confidence interval; *R*, reference category.

thicker choroid than the other two groups); higher IOP; and thicker CCT (Table 4). Even after adjusting for AL, diagnosis was significantly associated with CT ($P = 0.01$). Pairwise comparisons showed that the AC group had a significantly greater CT than both the normal group ($P = 0.003$) and the OA group ($P = 0.03$), but no significant difference was observed between the normal and OA groups ($P = 0.18$).

Since AL and ACD were significantly shorter in the overall AC group than in OA or normal groups, we performed an additional multivariable analysis (including all participants) in which we excluded AL and ACD. In this model, diagnosis was even more significantly associated with CT ($P < 0.0001$ compared with $P = 0.01$), with the AC group having a significantly greater CT than the normal group ($P < 0.0001$) and the OA group ($P < 0.0001$; Table 5). Furthermore, thicker CCT was no longer significantly associated with thinner CT, while higher IOP and older age remained significantly associated with thinner CT ($P = 0.02$ and $P < 0.0001$, respectively).

Table 4. Choroidal Thickness, Multivariable Analysis, All Participants ($N = 210$)

Characteristic	CT, μm: Regression Parameter (95% CI)	P Value
Age (per 5 y greater)	−16.3 (−21.1, −11.6)	<0.0001
AL (per mm greater)	−32.1 (−40.0, −24.2)	<0.0001
Diagnosis		
Normal (*R*)	0	0.01
POAGS/POAG	20.7 (−9.6, 51.0)	
PACS/PAC/PACG	51.2 (18.1, 84.3)	
IOP (per 10 mm Hg greater)	−26.3 (−49.2, −3.4)	0.02
CCT (per 100 μm greater)	−31.8 (−60.2, −3.5)	0.03

R square = 0.4480.

P values for pairwise comparisons of diagnosis: normal versus POAGS/POAG = 0.18; normal versus PACS/PAC/PACG = 0.003; POAGS/POAG versus PACS/PAC/PACG = 0.03.

Table 5. Choroidal Thickness, Multivariable Analysis Excluding Axial Length and ACD, All Participants ($N = 210$)

Characteristic	CT, μm: Regression Parameter (95% CI)	P Value
Diagnosis		
Normal (*R*)	0	<0.0001
POAGS/POAG	5.7 (−28.7, 40.1)	
PACS/PAC/PACG	95.8 (60.0, 131.5)	
Age (per 5 y greater)	−15.7 (−21.1, −10.3)	<0.0001
IOP (per 10 mm Hg greater)	−31.6 (−57.8, −5.5)	0.02
CCT (per 100 μm greater)	−27.3 (−59.8, 5.1)	0.10

R square = 0.2737.

P values for pairwise comparisons of diagnosis: normal versus POAGS/POAG = 0.74; normal versus PACS/PAC/PACG = <0.0001; POAGS/POAG versus PACS/PAC/PACG = <0.0001.

In our previous report, we found that diastolic PP was significantly associated with CT in a group of glaucoma patients and suspects.[9] When diastolic PP was included in a multivariable model including all participants (leaving out all other PP and BP terms as well as IOP), diastolic PP was not significantly associated with CT ($P = 0.20$). Similarly, when systolic and mean PP were included in separate multivariable models while leaving out all other PP and BP terms and IOP, neither PP variable was found to be significantly associated with CT.

We analyzed overall OA and AC patients without the normal subjects in a multivariable model to evaluate the association between CT and two measures of glaucoma damage: CDR and visual field MD (Table 6). Neither CDR nor visual field MD was found to be significantly associated with CT in this model.

Multivariable analysis for CT among only normal eyes identified longer AL as the only factor associated significantly with thinner CT (17 μm per mm increase in AL when adjusted for age, $P = 0.04$). Age was somewhat, but not significantly, associated with CT (–9 μm per 5-year increase in age, $P = 0.08$).

Discussion

In this prospective study of 225 participants, including 40 normals, AC diagnosis was associated with a thicker choroid

Table 6. Choroidal Thickness, Multivariable Analysis, OA and AC Participants ($N = 170$)

Characteristic	CT, μm: Regression Parameter (95% CI)	P Value
Age (per 5 y greater)	−13.6 (−19.3, −7.9)	<0.0001
AL (per mm greater)	−37.9 (−45.4, −30.4)	<0.0001
IOP (per 10 mm Hg greater)	−34.6 (−58.6, −10.6) 0.005	0.005
Pseudophakic eye		
No (*R*)	0	0.04
Yes	−43.9 (−76.4, −11.3)	

R square = 0.4803.

while older age, longer AL, higher IOP, and thicker CCT were associated with a thinner choroid. Several other investigations of factors associated with CT have also determined that older persons and eyes with longer AL or myopic refraction have a thinner choroid.[9–13] Our present results confirm most of the features associated with CT from our previous report, where AC diagnosis was associated with greater CT and older age, longer AL, and thicker CCT were associated with thinner CT.[9] To our knowledge, there are no other publications evaluating CT among OA, AC, and normal persons.

AC eyes had a thicker choroid when compared with OA and normal eyes, even after adjusting for the shorter AL in AC eyes. Furthermore, in a recent study comparing the response of OA and AC eyes in the water-drinking test (WDT),[17] we found that 30 minutes after rapidly drinking 1 L of water, there was a significantly greater increase in CT and in IOP in AC than in OA eyes. This greater increase in CT in AC eyes occurred despite the increase in IOP in these eyes, which would be expected to cause thinning of the choroid, all other factors being equal.[17] This suggests that in addition to having a significantly thicker choroid at baseline, AC eyes have a greater tendency to dynamic change in CT than do OA eyes.[17]

The significantly greater baseline CT and the greater tendency to choroidal expansion in AC eyes may be related to the development of AC disease.[30–32] For example, choroidal expansion participates in secondary AC after central retinal vein occlusion or after scleral buckling procedures.[33] Recent UBM studies of AC eyes show abnormal separations between the choroid and sclera, an observation consistent with the idea that choroidal expansion contributes to the development of AC.[34–35] Clinical observations also suggest that intra- and postoperative choroidal expansion is more common in extreme cases of AC disease, such as nanophthalmos. We hypothesize that choroidal expansion contributes to the process of AC by the following sequence of events. The intraocular volume increase coincident with choroidal expansion causes an immediate increase in IOP.[30–32] As a result of this IOP increase, trabecular aqueous outflow would likely increase in order to restore IOP toward normal.[30–32] A posterior to anterior pressure differential would result as fluid left the anterior chamber, and aqueous volume in the anterior chamber would decrease.[30–32] The lens would then move forward, narrowing the iris-lens channel and intensifying resistance to aqueous movement through the pupil (pupillary block).[30–32] Using Navier-Stokes equations of fluid dynamics, we have previously demonstrated that in the AC eye, even an anterior lens movement of a few μm could result in an increased transiris pressure differential,[36] leading the iris to bow forward to make contact with the meshwork. Thus, in the predisposed eye with a baseline narrow angle, dynamic expansion of the choroid would contribute to a greater chance for symptomatic or asymptomatic AC.[30–32]

In our previous report, we also found that the combination of lower BP or higher IOP, expressed as lower diastolic PP, was associated with a thinner choroid.[9] In the present expanded group of eyes, higher IOP was associated with thinner CT, while PP was not a significant variable. Polska et al. have shown that human choroidal blood flow is maintained in the face of changes in ocular PP, including both mean arterial pressure and IOP.[37,38] This autoregulation seems more efficient with changes in blood pressure than with changes in IOP.[37,38] Prior work in animals had also demonstrated that the autoregulatory capacity of choroidal blood flow was less effective with changes in IOP compared with changes in BP.[39] Although our finding is from a cross-sectional comparison, it is compatible with these studies, since less effective autoregulation would allow greater changes in choroidal blood volume and CT with changes in IOP than with changes in BP. It is logical that higher IOP would reduce choroidal blood volume and CT. Consistent with this hypothesis, although AC eyes had an expansion of the choroid during the WDT, those eyes with greater IOP increase had less choroidal expansion.[17]

Interestingly, CCT, which has been linked to several aspects of ocular anatomy and physiology, including a greater risk of OAG,[40] was also found to be inversely associated with CT in the multivariable model in all patients (Table 4). However, when AL and ACD were excluded from the list of factors being considered for the multivariable model, CCT was no longer associated significantly with CT (Table 5). We speculate that the association of CCT with CT may somehow be related to AL and ACD. Further research is needed to clarify the relationships among these factors.

Among the 40 normal subjects in our study, we found that longer AL was the only factor significantly associated with thinner CT, while the association between older age and thinner CT was of borderline significance. Several groups have reported thinner CT with older age in normals,[11,25,41,42] while at least two groups have found an association between thinner CT and longer AL or myopic refractive error.[11,43] It is interesting that other factors found to be associated with CT in our multivariable analysis among all patients (Table 4), such as CCT and IOP, were not found to be associated with CT among normals considered alone. It is possible that a larger sample of normals would allow detection of associations between CT and these other factors. However, it is also possible that these features are inherently related to OA or AC glaucoma.

Our data do not support the idea that glaucoma damage is associated with a thinner choroid, as had been suggested by prior histological studies.[22–24] First, no significant difference in CT was found between normals and the OA group or between the POAGS and POAG groups. Furthermore, neither visual field MD nor CDR was found to be associated with CT in the multivariable analysis among glaucoma patients (Table 6). Several other studies have found no association between glaucoma damage and CT as measured by SD-OCT.[25–28] It is important for studies that evaluate relationships between CT and disease states to account for the important variables that may confound such assessments, such as age, AL, CCT, BP, and IOP.

The limitations of our study include the possibility that the glaucoma patients at a referral center may differ from a population-based sample of individuals with glaucoma. However, we have no reason to believe that they are unrepresentative. Second, we measured the choroid in the posterior 6 mm of the eye. It is possible that other areas of the choroid might have different thicknesses, though at present the ability of commercial SD-OCT instruments to measure the peripheral choroid is limited. We were not able to obtain ideal images of the choroid in 12% of the macular scans. The visualization of the CSI will undoubtedly improve with further developments in technology.

In summary, we found that factors that were significantly associated with a thinner choroid were older age, longer AL, higher IOP, and thicker CCT. AC subjects had a thicker choroid than OA and normal subjects, even after adjusting for the shorter AL in AC eyes. This observation supports hypotheses suggesting that choroidal expansion is a contributing factor to the development of AC disease. Finally, we found that CT is not related to the degree of glaucoma injury.

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