Clinical and Epidemiologic Research

Subfoveal Choroidal Thickness in 1323 Children Aged 11 to 12 Years and Association With Puberty: The Copenhagen Child Cohort 2000 Eye Study

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Purpose. To investigate subfoveal choroidal thickness and ocular- and systemic-associated factors in a population-based cohort of children.

Methods. Cross-sectional, observational study where 1323 healthy 11- and 12-year-old children were examined with enhanced-depth imaging spectral-domain optical coherence tomography (EDI-SD-OCT), ocular interferometric biometry, blood pressure manometry, and measurement of height, weight, nonmydriatic refraction, and best-corrected visual acuity. Self-reported stage of pubertal development was classified as Tanner stages 1 through 4.

Results. Mean subfoveal choroidal thickness was 369 ± 81 µm in girls and 348 ± 72 µm in boys. Longer axial length was associated with a thinner subfoveal choroid (−27.2 [95% confidence interval (CI) −32.7 to −21.7] µm/mm; $P < 0.0001$), adjusting for age and sex. There was no difference in choroidal thickness between sexes ($P = 0.14$) after adjusting for age and axial length. In girls, the choroid was thickest in participants in the more advanced stage of pubertal development (54.2 [95% CI 20.7–87.7] µm for Tanner 4 versus Tanner 1, $P = 0.0015$) and increased with body height (19.2 [95% CI 10.8–27.5] µm/10 cm, $P < 0.0001$). There was no effect of height or puberty in boys, who were less sexually mature than girls.

Conclusions. Choroidal thickness in girls increased with body height and sexual maturation. The results suggest that puberty promotes choroidal thickening in girls, an effect that may be mediated by the pubertal growth spurt. The lack of pubertal effect in boys may be related to a smaller proportion of boys in this study having entered puberty.

Keywords: choroidal thickness, children, optical coherence tomography, puberty development, axial length, population study, EDI-OCT, OCT

Enhanced depth imaging spectral-domain optical coherence tomography (EDI-SD-OCT)[1] has enabled noninvasive visualization and quantitative assessment of the choroid. Measurement of the choroidal thickness has been shown to be clinically relevant in diseases such as central serous chorioretinopathy[2] and Vogt-Koyanagi-Harada disease[3] (associated with thicker choroids), as well as myopia,[4–6] diabetic retinopathy,[7] and AMD[8] (associated with thinner choroids). In adults, subfoveal choroidal thickness also associates with age,[1,9,10] refraction,[9,10] axial length,[9,10] sex,[10–13] time of day,[14] and systolic blood pressure.[14] Age, myopic refractive error, and axial length[1,9,10] are the most frequently and consistently observed associations with decreasing choroidal thickness in healthy adults. A tipping point for the age-related attenuation of the subfoveal choroid has been reported at 30 years in one study[15] and at 60 years in another study.[16] Studies of choroidal thickness in children have found conflicting results. Thus, a study of 54 healthy Korean children found a decrease in subfoveal choroidal thickness with age, but no significant correlation between choroidal thickness and axial length or refraction.[17] A study of 194 emmetropic Australian children found an increase in choroidal thickness from 4 to 6 years to 7 to 9 years of age, but little difference between 7 to 9 years and 10 to 12 years.[18] Another recent study reported thinner choroid in myopic children, especially at the central fovea region.[19] In combination, age, refractive error, and axial length account for only a minor proportion of the variation in choroidal thickness in children, suggesting that other factors may be involved.[17–20]

The purpose of this report was to describe subfoveal choroidal thickness and its ocular and systemic associations with height, weight, body mass index, and pubertal development in a cohort of 11- to 12-year-old children.

Methods

Subjects

The Copenhagen Child Cohort 2000 Eye Study is a prospective, population-based, observational study, the baseline examination of which was an appendix to the 11-year follow-up of the Copenhagen Child Cohort 2000 study (CCC2000, formerly known as the Copenhagen County Child Cohort[21]), a prospective longitudinal study of child mental health, comprising a basic study population of the 6090 children born in the year 2000 in 16 selected municipalities in the Copenhagen County. The CCC2000 is representative of the Danish population.[22]

Of the 1632 children who attended face-to-face mental health assessment in the core study at age 11 to 12 years, 1406 children (86.2%) and their parents or legal guardians volunteered for the child to participate in the supplementary eye study. Exclusion criteria included previous eye trauma ($n = 9$), congenital malformation of the eye ($n = 1$), corrected visual acuity less than 80 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at 4-m distance (Snellen 0.8; $n = 14$), missing axial length measures ($n = 11$), missing or poor quality EDI-SD-OCT scans ($n = 13$), and an inability to cooperate during the eye examination ($n = 35$). This led to 83 children being excluded from the analysis. Only right eyes were included. The study was approved by the local medical ethics committee and performed in accordance with the Declaration of Helsinki. Informed consent was obtained from children's parents or legal guardians prior to examinations.

All participants were asked about current and previous ophthalmic disease or disorder and treatments. Past medical history and information about current medication use were obtained from the parents. Height without shoes was measured using a metal column height–measuring stand (Height Measuring Rod 5003; Soehnle Professional GmbH & Co., Backnang, Germany) to the nearest 0.1 cm. Weight was measured using an electronic scale (Exact/personal scale 6295; OBH Nordica Denmark A/S, Taastrup, Denmark) to the nearest 0.1 kg. Puberty stage was assessed by presentation to the child of diagrams showing the Tanner stages 1 through 4 and asking the child to point out which diagram best illustrated the child's stage of physical development. Arterial blood pressure was measured after 5 minutes of rest in the seated position using an automated sphygmomanometer (Omron HEM 705 LP; Omron Healthcare, Inc., Kyoto, Japan) with a cuff dimensioned for children. Two separate measurements were obtained and their average was calculated and used for analysis. Height, weight, Tanner stage, and blood pressure were obtained before the ophthalmic examination.

The study design gave priority to representativity and recruitment over cycloplegia, based on the rationale that administration of eye drops would reduce and skew recruitment and that information about axial length can substitute, to some extent, for information that would otherwise have to be obtained by cycloplegic refractioning. Visual acuity and best-corrected visual acuity were determined using ETDRS charts and an abbreviated refraction protocol where refractioning was pursued only until the participant saw 80 ETDRS letters or better. Noncycloplegic objective refraction measured by an automated refractometer (Retinomax K-plus 2; Right MFG Co., Ltd., Tokyo, Japan) was used to guide refractioning. Ocular axial length and anterior chamber depth were measured using an interferometry-based instrument (IOL-Master, version 3.01.0294; Carl Zeiss Meditec, La Jolla, CA) and calculated as the average of at least five and three scans, respectively. Multipeaked biometric measurements were repeated until multipeaked features had disappeared or, if they did not, the data were omitted from analysis.

The posterior segment of the eye was imaged using EDI-SD-OCT (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany). Eye tracking and automated real-time averaging features were used. Two fovea-centered scan protocols were used, one with seven horizontal lines within a $5° \times 30°$ rectangle and the second with a 4-line radial scans at 30°. Each aligned line scan represents the average of 25 B-scans. The grader chose the horizontal line scan believed to best represent the foveal center as judged from the presence of a pronounced foveal center specular reflex and the deepest foveal depression. Subfoveal choroidal thickness was then measured using the instrument manufacturer's software (Heidelberg Eye Explorer, version 1.6.1.0; Heidelberg Engineering). The segmentation line depicting the inner limiting membrane was moved manually to the choroidoscleral border by an experienced operator (XQL). Intergrader variability has previously been assessed[11] and was not measured again in the current study. When a suprachoroidal space was visible, the segmentation line was fitted to the border between the suprachoroidal space and the sclera. Scans with a signal-to-noise ratio poorer than 25 dB were rejected. The choroidoscleral boarder was visible and subfoveal choroidal thickness measurable in all 1323 children included in this study.

Statistical analyses were made using SAS software (ver. 9.2; SAS Institute, Cary, NC). Means and SDs were calculated for continuous variables and medians and interquartile ranges for skewed distributions. Comparisons between sexes were made using two-tailed Student's *t*-tests or χ^2 tests (Tanner stages). Association between choroidal thickness and parameters were assessed using a general linear model. Tanner stages were entered as ordinal data. Age was calculated in days but in results presented in years. Axial length, anterior chamber depth, spherical equivalent refractive error, visual acuity, height, weight, body mass index, systolic, and diastolic blood pressure were included as continuous variables. Spherical equivalent refraction was calculated as the algebraic sum of the value of the sphere and half the cylinder. Tests for interactions with sex were performed by adding the cross product to the model. The assumptions of linearity, variance homogeneity, and normality of the distribution of residuals underlying the statistical model were assessed by display of relevant plots and reviewed by a statistical consultant. Multivariate regression analysis was performed including parameters that were significantly associated with subfoveal choroidal thickness in the univariate analyses. The level of statistical significance was set to P less than 0.05, and estimates presented with 95% confidence intervals (95% CI).

Results

The criteria for inclusion in analysis were met by 1323 children (52.2% girls, 47.8% boys; Table 1). Girls and boys were of comparable age ($P = 0.88$; Table 1). Mean best-corrected visual acuity was 89 ± 3 ETDRS letters for both girls and boys (Snellen equivalent 1.2) and noncycloplegic spherical equivalent refraction was comparable (0.1 ± 0.8 D; $P = 0.60$; Table 1). The girls were significantly taller than boys, with a mean height of 152.5 ± 7.4 cm for girls compared with 151.4 ± 7.5 cm for boys ($P = 0.011$), but girls had a shorter mean axial length of 22.9 ± 0.7 mm compared with 23.5 ± 0.7 mm in boys ($P < 0.0001$), and a shallower anterior chamber of 3.47 ± 0.2 mm vs. 3.56 ± 0.2 mm ($P < 0.0001$; Table 1). Tanner stages were available in 1274 children. More girls than boys had entered puberty, 26 out of 663 girls (3.9%) being in Tanner stage 4 compared with 7 out of 611 boys (1.1 %; Table 1). Mean weight, body mass index, and systolic and diastolic blood pressure were comparable in girls and boys.

Mean subfoveal choroidal thickness was 369 ± 80.8 (range, 164–650) μm in girls, which was significantly thicker than in boys, who had a mean subfoveal choroidal thickness of 348 ± 72.1 (range, 164–586) μm ($P < 0.0001$; Table 1). Subfoveal choroidal thickness decreased with increasing axial length ($P < 0.0001$; Table 2; Fig. 1) and with increasing anterior chamber depth ($P = 0.047$), and increased with increasing hyperopic spherical equivalent refraction ($P < 0.0001$) and with age ($P = 0.046$; Table 2).

Table 1. Demographic Characteristics of the 1323 Study Participants

Parameter	Boys, *n* = 633	Girls, *n* = 690	*P*
Age, y	11.7 (0.4)	11.7 (0.4)	0.88
Visual acuity, letters	89 (3)	89 (3)	0.06
Refractive error, D	0.1 (0.8)	0.1 (0.8)	0.60
Axial Length, mm	23.5 (0.7)	22.9 (0.7)	<0.0001
Anterior chamber, mm	3.56 (0.2)	3.47 (0.2)	<0.0001
Height, cm	151.4 (7.5)	152.5 (7.4)	0.011
Weight,* kg	42.4 (8.9)	43.2 (8.9)	0.11
Body mass index, kg/m²	18.4 (2.9)	18.5 (3.1)	0.64
Blood pressure systolic, mm Hg	115 (9.6)	116 (10.0)	0.21
Blood pressure diastolic, mm Hg	65 (7.9)	65 (7.1)	0.69
Subfoveal choroid, µm	348 (72.1)	369 (80.8)	<0.0001
Puberty development, Tanner stage†	*n* = 611	*n* = 663	–
Tanner 1	161 (26.4%)	122 (18.4%)	–
Tanner 2	334 (54.7%)	331 (49.9%)	–
Tanner 3	109 (17.8%)	184 (27.8%)	–
Tanner 4	7 (1.1%)	26 (3.9%)	<0.0001

Refractive error, spherical equivalent refractive error. Values are mean (SD).
* Value is median (interquartile range).
† For Tanner stages the values are number (column percent).

When controlling for axial length and age there was no significant difference in subfoveal choroidal thickness between girls and boys ($P = 0.14$; Table 2). The association between choroidal thickness and anterior chamber depth flipped to a deeper anterior chamber being associated with a thicker subfoveal choroid (28.9 [95% CI 8.9–48.8] µm/mm; $P = 0.0046$) after adjusting for age, sex, and axial length (Table 2). Adjusting for age and sex did not affect the association between axial length and subfoveal choroidal thickness, which decreased by 27.2 µm/mm increase in axial length (95% CI 32.7–21.7 µm/mm; $P < 0.0001$) and subfoveal choroidal thickness remained associated with age when controlling for sex and axial length ($P = 0.019$; Table 2). The association between refraction and subfoveal choroidal thickness remained significant when controlling for axial length, age, and sex (6.8 [95% CI 1.1–12.5] µm/D; $P = 0.020$; Table 2).

The effect of height, weight, and Tanner stages on choroidal thickness differed between sexes with interaction terms of $P = 0.0086$, $P = 0.016$, $P = 0.057$, respectively. Girls in Tanner stage 4 had 54.2 µm thicker subfoveal choroids compared with the

Table 2. Subfoveal Choroidal Thickness and Associated Factors in Children

	Crude Data			Adjusted for Age, Axial Length, and Sex		
Parameter	Estimate, 95% CI	*P*	R^2	Estimate, 95% CI	*P*	R^2†
Age, µm/y	10.6 (0.2 to 21.0)	0.046	0.003	11.9 (1.9 to 21.7)	0.019	0.004
Sex, girls vs. boys, µm	20.6 (12.3 to 28.9)	<0.0001	0.018	6.4 (−2.1 to 14.9)	0.14	–
Axial length, µm/mm	−28.5 (−33.7 to −23.2)	<0.0001	0.080	−27.2 (−32.7 to −21.7)	<0.0001	0.064
Anterior chamber, µm/mm	−18.8 (−37.4 to −0.3)	0.047	0.003	28.9 (8.9 to 48.8)	0.0046	0.005
Refractive error, µm/D	17.1 (11.8 to 22.3)	<0.0001	0.030	6.8 (1.1 to 12.5)	0.020	0.004
Visual acuity, µm/letter	−0.4 (−2.0 to 1.2)	0.65		0.8 (−0.6 to 2.5)	0.24	–
Body mass index, µm	0.5 (−1.0 to 1.9)	0.52		0.6 (−0.8 to 1.9)	0.42	–
Systolic blood pressure, 10 mm Hg	1.4 (−3.1 to 5.8)	0.54		1.6 (−2.6 to 5.9)	0.45	–
Diastolic blood pressure, 10 mm Hg	0.5 (−6.3 to 5.3)	0.87		1.1 (−4.4 to 6.7)	0.69	–
Subfoveal choroidal thickness and height, weight, and Tanner staging, stratified by sex*						
Boys						
Height, µm/10 cm	−0.3 (−7.9 to 7.3)	0.94		1.7 (−6.1 to 9.6)	0.66	–
Weight, µm/kg	−0.2 (−0.9 to −0.4)	0.48		−0.1 (−0.7 to 0.6)	0.77	–
Tanner 2 vs. 1	−1.8 (−15.5 to 11.9)	0.80		−4.3 (−17.8 to 9.2)	0.53	–
Tanner 3 vs. 1	−2.7 (−20.4 to 15.1)	0.77		−4.8 (−22.9 to 13.3)	0.60	–
Tanner 4 vs. 1	−25.3 (−80.6 to 29.9)	0.37		−13.9 (−67.8 to 39.9)	0.53	–
Girls						
Height, µm/10 cm	14.5 (6.4 to 22.7)	0.0005	0.018	19.2 (10.8 to 27.5)	<0.0001	0.022
Weight, µm/kg	0.9 (0.2 to 1.5)	0.0072	0.011	1.0 (0.4 to 1.7)	0.0019	0.011
Tanner 2 vs. 1	1.7 (−15.0 to 18.3)	0.84		3.0 (−13.4 to 19.4)	0.72	–
Tanner 3 vs. 1	14.4 (−3.9 to 32.8)	0.12		15.1 (−3.3 to 33.4)	0.11	–
Tanner 4 vs. 1	56.8 (22.9 to 90.7)	0.0011	0.021	54.2 (20.7 to 87.7)	0.0015	0.012

Refractive error, spherical equivalent refractive error.
* The association between subfoveal choroidal thickness and height, weight, and Tanner staging are analyzed separately for girls and boys due to interaction between sex and height ($P = 0.0086$), sex and weight ($P = 0.016$), and sex and Tanner ($P = 0.057$).
† R^2 for the individual parameters, adjusted for R^2 for age, axial length, and sex ($R^2 = 0.085$).

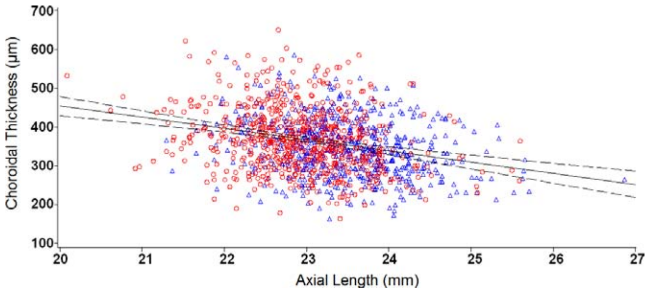

Figure 1. Subfoveal choroidal thickness as a function of axial length in girls (*red circles*) and boys (*blue triangles*). Regression line (β = –28.5 µm/mm axial length; 95% CI –33.7 to –23.2 µm; $P < 0.0001$; *black*) is displayed with 95% CI.

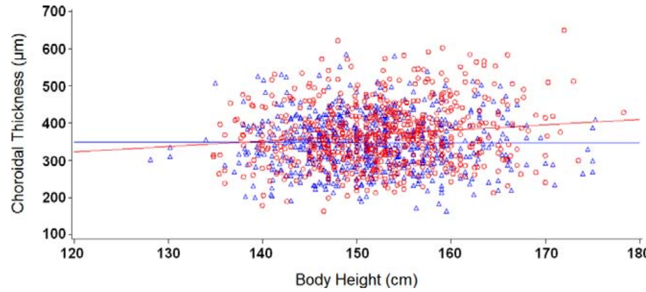

Figure 3. Subfoveal choroidal thickness as a function of body height in girls (β = 14.5 µm/10 cm body height; 95% CI 6.4–22.7; $P = 0.0005$; *red circles*) and boys (β = –0.3 µm/10 cm body height, $P = 0.94$; *blue triangles*). There was a significant interaction between sex and body height ($P = 0.0086$) on subfoveal choroidal thickness.

prepubertal girls in Tanner stage 1 (95% CI 20.7–87.7 µm; $P = 0.0015$; Table 2; Fig. 2) and the subfoveal choroidal thickness in girls increased with height by 19.2 µm/10 cm (95% CI 10.8–27.5 µm/10 cm; $P < 0.0001$; Table 2; Fig. 3) and with weight by 1.0 µm/kg (95% CI 0.4–1.7 µm/kg; $P = 0.0019$; Table 2) when adjusting for age and axial length. Subfoveal choroidal thickness was not associated with height, weight, or Tanner stage in boys (Table 2; Figs. 2, 3). There was no significant interaction between age and sex ($P = 0.21$). If stratified by sex and adjusted for axial length, however, subfoveal choroidal thickness was significantly associated with age (16.9 [95% CI 2.6–31.3] µm/y; $P = 0.021$) in girls, but not in boys (3.36 [95% CI –10.8 to 17.6] µm/y; $P = 0.39$; data not tabulated).

In the multivariate analysis stratified on sex including all significant associated factors, subfoveal choroidal thickness in girls remained significantly associated with height (20.0 [95% CI 8.9–31.2] µm/10 cm; $P = 0.0005$; Table 3), while there was only a tendency for thicker subfoveal choroids in girls in Tanner stage 4 compared with Tanner stage 1 ($P = 0.055$; Table 3). Age and weight showed no independent effect on subfoveal choroidal thickness ($P > 0.05$). Axial length remained significantly associated with subfoveal choroidal thickness in the multivariate analysis in both girls and boys ($P < 0.0001$; Table 3). A deeper anterior chamber was associated with a thicker subfoveal choroid only in boys ($P = 0.0032$; Table 3). Higher hyperopic refractive error was associated with a thicker subfoveal choroid only in girls ($P = 0.0030$; Table 3).

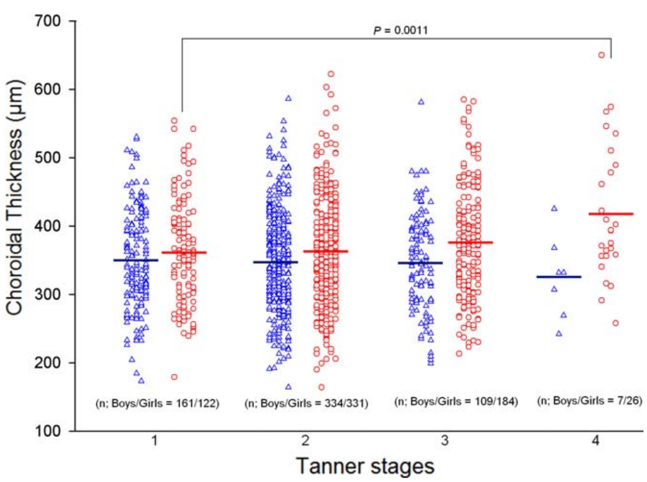

Figure 2. Subfoveal choroidal thickness in girls (*red circles*) and boys (*blue triangles*) by self-reported Tanner stage of puberty 1 to 4 according to genital, breast, and pubic hair development. Girls in the Tanner stage 4 had 56.8 µm thicker subfoveal choroids than girls in Tanner stage 1 (95% CI 22.9–90.7; $P = 0.0011$).

Subfoveal choroidal thickness was not associated with best-corrected visual acuity, systolic or diastolic blood pressure or body mass index in any of the models (Table 2).

Discussion

In this population-based cohort of 11- and 12-year-old children, mean subfoveal choroidal thickness was thicker in girls than in boys, but the difference was not significant when controlling for axial length, which was strongly associated with subfoveal choroidal thickness in both sexes. More advanced puberty development and increasing body height were associated with thicker subfoveal choroid in girls but not in boys, of whom few had reached the more advanced puberty stages.

The present study is, to the best of our knowledge, the largest population-based cohort of children examined with EDI-SD-OCT and assessed for subfoveal choroidal thickness. The manual segmentation technique used in this study may in time be superseded by automated methods for choroidal thickness measurement,[23] but currently there is no established ulterior method and no better reference than visual evaluation by a human grader. Subfoveal choroidal thickness in the current study was graded by a single observer with prior experience to promote uniformity of the grading process and avoidance of learning curve effects. High intra-observer and interobserver reproducibility has been shown in a population-based study of subfoveal choroidal thickness in 3233 Chinese adults.[24] Limitations of this study include lack of cycloplegic refractioning and absence of IOP data. Cycloplegic drops were avoided to optimize recruitment for the eye study, which was 86.2% of the cohort attending the core CCC2000 Study examination in 2011 to 2012. Pubertal development was assessed by self-reporting, which may be considered a reasonably accurate method despite a potential for underestimation at later stages of maturation.[25] Finally, no conclusion about causality can be made because of the cross-sectional design of this baseline examination data analysis.

Both the mean and the variation of subfoveal choroidal thickness found in the present study are in good agreement with previous studies of choroidal thickness in children.[17–20] We found a strong association of axial length with subfoveal choroidal thickness, the latter decreasing with increasing axial length as in previous studies in children[18] and young adults.[11] Also in line with previous studies[9,10] we found increasing hyperopic refraction error to be associated with increasing choroidal thickness. The association was still present when including axial length in the analysis. The association between anterior chamber depth and choroidal thickness was inverted when adjusting for axial length. It should be noted that because we did not induce cycloplegia, accommodation of

Table 3. Multivariate Analysis of Associations With Subfoveal Choroidal Thickness

Parameter	Boys		Girls	
	Estimate, 95% CI	P	Estimate, 95% CI	P
Age, μm/y	6.9 (−9.2 to 23.1)	0.40	1.9 (−14.0 to 17.8)	0.81
Axial length, μm/mm	−27.4 (−37.6 to −17.3)	<0.0001	−28.1 (−38.2 to −17.9)	<0.0001
Anterior chamber, μm/mm	44.1 (14.9 to 73.3)	0.0032	22.4 (−6.1 to 50.8)	0.12
Refractive error, μm/D	6.7 (−1.8 to 15.2)	0.12	12.9 (4.4 to 21.5)	0.0030
Height, μm/10 cm	4.1 (−6.7 to 14.8)	0.45	20.0 (8.9 to 31.2)	0.0005
Weight, μm/kg	−0.2 (−1.1 to 0.6)	0.59	−0.3 (−1.2 to 0.6)	0.56
Puberty development, $n = 1274$, μm				
Tanner 2 vs. 1	−4.4 (−18.7 to 10.0)	0.55	−4.6 (−22.1 to 12.9)	0.60
Tanner 3 vs. 1	−6.2 (−25.6 to 13.3)	0.53	2.3 (−18.5 to 23.0)	0.83
Tanner 4 vs. 1	−21.3 (−79.4 to 36.7)	0.47	36.7 (−0.8 to 74.2)	0.055

Refractive error, spherical equivalent refractive error. Adjusted for all variables listed. R^2 for boys: 0.083; R^2 for girls: 0.121.

undocumented amplitude may have affected the associations between refraction and anterior chamber depth.

Differences in choroidal thickness between women and men have previously been reported, men having a thicker choroid than women.[10–13] In healthy university students, we found thicker choroids in men than in women for the same ocular axial length.[11] In the present study of prepubertal children and children, some of whom recently entered puberty, we did not find a significant difference in choroidal thickness between boys and girls after adjusting for the effect of axial length, a discrepancy that appears to be explained by earlier onset of puberty in girls.

In girls, choroidal thickness increased with the stage of pubertal development and with height and weight. When including all variables, only height remained significantly associated. The three factors are biologically interconnected because puberty is accompanied by a growth spurt with large increases in height and weight.[26] Consequently, height may have been a better measure of pubertal development in the present study than the self-reported Tanner stage. The ideal parameter to describe puberty may indeed be the rate of increase in height around the time of the examination, a parameter that we have not recorded. The most likely reason that we saw no effect of height, weight, or pubertal development in boys is that the boys were lagging behind the girls in pubertal development. Pubertal growth acceleration occurs roughly 2-years earlier in girls than in boys, peaking for girls around the age of 11 to 12 years of age.[27,28] Studies of older children, where both sexes have entered or completed puberty, are necessary to find out if choroidal thickness is also related to puberty in boys. The later onset but longer duration and larger growth amplitude of puberty in boys[26] may explain why men have thicker subfoveal choroids than women.[10–13]

Despite the narrow age range in the current study, we found that subfoveal choroidal thickness increased with age before including height in the analyses. Cross-sectional studies[15,17,20] with a broader age distribution but smaller numbers of children have reported a decrease in subfoveal choroidal thickness with age, while a study of 194 emmetropic Australian children aged 4 to 12 years[18] found an age-related increase in choroidal thickness. Our study suggests that discrepancies in rates of change in choroidal thickness with age in different studies of children may be explained by confounding effects of puberty.

Our data indicate that the choroid may grow to increasing thickness during puberty despite the eye undergoing axial elongation. Recent longitudinal studies in children and adolescents have reported concomitant pubertal growth spurting and axial length elongation, with variation between girls and boys in the time of onset and magnitude of change.[28,29] These observations suggest that the pubertal growth spurt and growth hormone surge may modulate myopia progression.[28] The earlier termination of puberty in women may explain which myopia, which is strongly related to having a thin choroid,[4–6] is more prevalent in women than in men in some population-based studies,[30–32] though not in all.[33,34] Myopia has indeed been reported to progress faster in young girls[35] and to be associated with early menarche in Indian women[36] and with body height in Singaporean girls.[37] The results of the present study indicate the existence of a relationship between height, pubertal development, and subfoveal choroidal thickness in girls aged 11 to 12 years. A follow-up study of boys who have entered puberty is necessary to determine if the same associations are present in boys.

Animal studies indicate that the choroid is actively involved in the emmetropization process.[38–40] Using mathematical modeling of the ocular development in children aged 10 to 15 years, it has been shown that myopic children have a thinner choroid that expected for a given axial length.[19] A popular model of emmetropization describes the choroid as a source of growth factors and a regulator of the access of growth factors secreted by the retina or RPE to the sclera.[38–40] Obviously, the role of the choroid in the development of myopia can best be investigated in longitudinal studies.

In conclusion, this study identified an effect of height and pubertal development on choroidal thickness in girls in a cohort of prepubescent and early pubescent 11- and 12-year-old children. The strong association between axial length and choroidal thickness found in adults was also present in these children. The impact of choroidal thickness on the development of myopia in children should be investigated in longitudinal studies. The results of the current study indicate that difference in stature and puberty development between the two sexes should be considered in studies of myopia in children.

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References

1. Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. *Am J Ophthalmol*. 2009;147:811–815.
2. Pryds A, Larsen M. Choroidal thickness following extrafoveal photodynamic treatment with verteporfin in patients with central serous chorioretinopathy. *Acta Ophthalmol*. 2012;90: 738–743.
3. Nakayama M, Keino H, Okada AA, et al. Enhanced depth imaging optical coherence tomography of the choroid in Vogt-Koyanagi-Harada disease. *Retina*. 2012;32:2061–2069.
4. Flores-Moreno I, Lugo F, Duker JS, Ruiz-Moreno JM. The relationship between axial length and choroidal thickness in eyes with high myopia. *Am J Ophthalmol*. 2013;155:314–319.
5. Ho M, Liu DT, Chan VC, Lam DS. Choroidal thickness measurement in myopic eyes by enhanced depth optical coherence tomography. *Ophthalmology*. 2013;120:1909–1914.
6. Ikuno Y, Tano Y. Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2009;50:3876–3880.
7. Esmaeelpour M, Brunner S, Ansari-Shahrezaei S, et al. Choroidal thinning in diabetes type 1 detected by 3-dimensional 1060 nm optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2012;53:6803–6809.
8. Manjunath V, Goren J, Fujimoto JG, Duker JS. Analysis of choroidal thickness in age-related macular degeneration using spectral-domain optical coherence tomography. *Am J Ophthalmol*. 2011;152:663–668.
9. Ikuno Y, Kawaguchi K, Nouchi T, Yasuno Y. Choroidal thickness in healthy Japanese subjects. *Invest Ophthalmol Vis Sci*. 2010;51:2173–2176.
10. Wei WB, Xu L, Jonas JB, et al. Subfoveal choroidal thickness: the Beijing Eye Study. *Ophthalmology*. 2013;120:175–180.
11. Li XQ, Larsen M, Munch IC. Subfoveal choroidal thickness in relation to sex and axial length in 93 Danish university students. *Invest Ophthalmol Vis Sci*. 2011;52:8438–8441.
12. Zeng J, Liu R, Zhang XY, et al. Relationship between gender and posterior pole choroidal thickness in normal eyes [in Chinese]. *Zhonghua Yan Ke Za Zhi*. 2012;48:1093–1096.
13. Barteselli G, Chhablani J, El-Emam S, et al. Choroidal volume variations with age, axial length, and sex in healthy subjects: a three-dimensional analysis. *Ophthalmology*. 2012;119:2572–2578.
14. Tan CS, Ouyang Y, Ruiz H, Sadda SR. Diurnal variation of choroidal thickness in normal, healthy subjects measured by spectral domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2012;53:261–266.
15. Fujiwara A, Shiragami C, Shirakata Y, et al. Enhanced depth imaging spectral-domain optical coherence tomography of subfoveal choroidal thickness in normal Japanese eyes. *Jpn J Ophthalmol*. 2012;56:230–235.
16. Ding X, Li J, Zeng J, et al. Choroidal thickness in healthy Chinese subjects. *Invest Ophthalmol Vis Sci*. 2011;52:9555–9560.
17. Park KA, Oh SY. Choroidal thickness in healthy children. *Retina*. 2013;33:1971–1976.
18. Read SA, Collins MJ, Vincent SJ, Alonso-Caneiro D. Choroidal thickness in childhood. *Invest Ophthalmol Vis Sci*. 2013;54: 3586–3593.
19. Read SA, Collins MJ, Vincent SJ, Alonso-Caneiro D. Choroidal thickness in myopic and nonmyopic children assessed with enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2013;54:7578–7586.
20. Ruiz-Moreno JM, Flores-Moreno I, Lugo F, et al. Macular choroidal thickness in normal pediatric population measured by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2013;54:353–359.
21. Skovgaard AM, Olsen EM, Houmann T, et al. The Copenhagen County child cohort: design of a longitudinal study of child mental health. *Scand J Public Health*. 2005;33:197–202.
22. Olsen EF, Skovgaard AM, Weile B, Jørgensen T. Risk factors for failure to thrive in infancy depend on the anthropometric definitions used: the Copenhagen County child cohort. *Paediatr Perinat Epidemiol*. 2007;21:418–431.
23. Tian J, Marziliano P, Baskaran M, Tun TA, Aung T. Automatic segmentation of the choroid in enhanced depth imaging optical coherence tomography images. *Biomed Opt Express*. 2013;4:397–411.
24. Shao L, Xu L, Chen CX, et al. Reproducibility of subfoveal choroidal thickness measurements with enhanced depth imaging by spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2013;54:230–233.
25. Coleman L, Coleman J. The measurement of puberty: a review. *J Adolesc*. 2002;25:535–550.
26. Rogol AD, Roemmich JN, Clark PA. Growth at puberty. *J Adolesc Health*. 2002;31:192–200.
27. Liu YX, Wikland KA, Karlberg J. New reference for the age at childhood onset of growth and secular trend in the timing of puberty in Swedish. *Acta Paediatr*. 2000;89:637–643.
28. Yip VC, Pan CW, Lin XY, et al. The relationship between growth spurts and myopia in Singapore children. *Invest Ophthalmol Vis Sci*. 2012;53:7961–7966.
29. Wang D, Ding X, Liu B, Zhang J, He M. Longitudinal changes of axial length and height are associated and concomitant in children. *Invest Ophthalmol Vis Sci*. 2011;52:7949–7953.
30. Bar Dayan Y, Levin A, Morad Y, et al. The changing prevalence of myopia in young adults: a 13-year series of population-based prevalence surveys. *Invest Ophthalmol Vis Sci*. 2005;46:2760–2765.
31. Wang Q, Klein BE, Klein R, Moss SE. Refractive status in the Beaver Dam Eye Study. *Invest Ophthalmol Vis Sci*. 1994;35: 4344–4347.
32. Sperduto RD, Seigel D, Roberts J, Rowland M. Prevalence of myopia in the United States. *Arch Ophthalmol*. 1983;101:405–407.
33. Wong TY, Foster PJ, Hee J, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. *Invest Ophthalmol Vis Sci*. 2000;41:2486–2494.
34. Lam CS, Goldschmidt E, Edwards MH. Prevalence of myopia in local and international schools in Hong Kong. *Optom Vis Sci*. 2004;81:317–322.
35. Pärssinen O, Lyyra AL. Myopia and myopic progression among schoolchildren: a three-year follow-up study. *Invest Ophthalmol Vis Sci*. 1993;34:2794–2802.
36. Nirmalan PK, Katz J, Robin AL, et al. Female reproductive factors and eye disease in a rural South Indian population: the Aravind Comprehensive Eye Survey. *Invest Ophthalmol Vis Sci*. 2004;45:4273–4276.
37. Saw SM, Chua WH, Hong CY, et al. Height and its relationship to refraction and biometry parameters in Singapore Chinese children. *Invest Ophthalmol Vis Sci*. 2002;43:1408–1413.
38. Summers JA. The choroid as a sclera growth regulator. *Exp Eye Res*. 2013;114:120–127.
39. Nickla DL, Wallman J. The multifunctional choroid. *Prog Retin Eye Res*. 2010;29:144–168.
40. Wallman J, Wildsoet C, Xu A, et al. Moving the retina: choroidal modulation of refractive state. *Vision Res*. 1995;35: 37–50.