Subfoveal Choroidal Thickness and Cerebrospinal Fluid Pressure: The Beijing Eye Study 2011

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Purpose. The venous choroidal blood drains through the superior orbital vein into the intracranial cavernous sinus. The cerebrospinal fluid pressure (CSFP) may thus influence the choroidal venous blood pressure. Since volume and thickness of the choroid depend on its pressure, we tested the hypothesis whether the subfoveal choroidal thickness (SFCT) is associated with CSFP.

Methods. The population-based Beijing Eye Study 2011 included 3468 individuals. A detailed ophthalmic examination was performed including spectral-domain optical coherence tomography (SD-OCT) with enhanced depth imaging for measurement of SFCT. The CSFP was calculated as CSFP (mm Hg) = 0.44 × Body Mass Index (kg/m²) + 0.16 × Diastolic Blood Pressure (mm Hg) − 0.18 × Age (years) − 1.91.

Results. Mean calculated CSFP was 8.8 ± 3.7 mm Hg and mean SFCT was 254 ± 107 μm. In multivariate analysis, SFCT was significantly associated with higher CSFP (P = 0.009; standardized coefficient β: 0.08; regression coefficient B: 2.27) after adjusting for lower age (P < 0.001; β: −0.36; B: −3.99), shorter axial length (P < 0.001; β: −0.37; B: −35.7), lower body mass index (P = 0.02; β: −0.05; B: −1.51), and higher corneal curvature radius (P < 0.001; β: 0.10; B: 41.1). In univariate analysis, SFCT increased by 9.2 μm (95% confidence interval: 8.3, 10.1) for each mm Hg increase in CSFP. In a reverse manner, CSFP was significantly associated with thicker SFCT (P < 0.001; β: 0.007; B: 0.21), after adjusting for region of habitation (P < 0.001; B: −0.31; β: −2.52), higher levels of glucose (P = 0.02; B: 0.10; β: 0.04) and triglycerides (P < 0.001; B: 0.13; β: 0.09), higher intraocular pressure (P < 0.001; B: 0.17; β: 0.12), and thinner lens (P < 0.001; B: −2.39; β: −0.22).

Conclusions. Thicker subfoveal choroid was associated with higher CSFP after adjustment for age, axial length, body mass index, and corneal curvature radius. This association may explain thicker SFCT measurements in the morning than evening. It shows the importance of the CSFP for the physiology of the eye.

Keywords: subfoveal choroidal thickness, cerebrospinal fluid pressure, translamina cribrosa pressure difference, axial length, Beijing Eye Study

As a highly vascularized structure between the sclera and Bruch’s membrane, the choroid is composed of the choriocapillaris, the middle layer of medium-sized vessels (Sattler’s layer) and the outer layer with large vessels (Haller’s layer), melanocytes interposed between the vessels of Sattler’s layer and Haller’s layer, a NADPH-diaphorase–positive and nitric oxide synthase–positive ganglion cell plexus located mainly in the temporal–central portion, connective tissue, and other cellular elements.1,2 The choroid is primarily or secondarily involved in the pathogenesis of many diseases of the posterior segment of the eye, such as age-related macular degeneration, polypoidal choroidal vasculopathy, central serous chorioretinopathy, and myopic retinopathy.3–10 The arterial blood supply of the choroid occurs mainly through the short posterior ciliary arteries, and the choroid receives approximately 95% of the ophthalmic artery blood.11 The drainage of the venous blood is carried out through the vortex veins and the superior orbital vein, which joins the intracranial cavernous sinus within the compartment of the cerebrospinal fluid pressure (CSFP). Since the pressure in the draining part of a system of communicating tubes influences the pressure in the main part of the system, the CSFP may influence the choroidal venous blood pressure. Since the volume and thus the thickness of the choroid depend on its pressure, we tested the hypothesis whether the subfoveal choroidal thickness (SFCT) is associated with the CSFP. We used the enhanced depth imaging (EDI) mode of optical coherence tomography (OCT) as described by Spaide and colleagues12 to measure the choroidal thickness. We chose a population-based study design to avoid the potential bias due to referral-related selection of study participants. Since measurement of CSFP is...
invasive, we estimated the CSFP from diastolic blood pressure, age, and body mass index, using a formula that was derived in a previous investigation on the relationship between these three parameters.\textsuperscript{13} \textsuperscript{15}

**METHODS**

The Beijing Eye Study 2011 is a population-based cross-sectional study in Northern China.\textsuperscript{14,15} The Medical Ethics Committee of the Beijing Tongren Hospital approved the study protocol and all participants gave informed consent according to the Declaration of Helsinki. The study was carried out in five communities in an urban district in the North of Central Beijing and in three communities in a rural region south of Beijing. All subjects living in the communities and fulfilling the inclusion criterion of an age of ≥50 years were eligible for the study. Of an eligible population of 4403 individuals fulfilling the only criterion of an age of ≥50 years, 3468 (78.8%) individuals (1963 [56.6%] women) participated in the eye examination. The study was divided into a rural part (1635 [47.1%] subjects; 943 [57.7%] women) and an urban part (1835 [52.9%] subjects; 1020 [55.6%] women). The mean age was 64.6 ± 9.8 years (median, 64 years; range, 50–95 years). The details of the Beijing Eye Study 2011 have been described recently.\textsuperscript{16}

All study participants underwent an interview with standardized questions on topics such as their family status, level of education, quality of life, known major systemic diseases, and quality of vision. Fasting blood samples were taken for measurement of blood lipids, glucose, and glycated hemoglobin HbA1c. Blood pressure was measured. Body height and weight and the circumference of the waist and hip were recorded. The ophthalmic examination included measurement of visual acuity with refractometry; tonometry; slit lamp examination of the anterior and posterior ocular segment; biometry of the right eyes (or of the left eyes if measurements of the right eye were not possible) (Lenstar 900 Optical Biometer; Haag Streit, Koeniz, Switzerland); and digital photography of the cornea, lens (slit lamp digital camera Type BG-i; Topcon Medical Systems, Inc., Tokyo, Japan); retro-illuminated lens photographs by Neitz CTR camera [Neitz Instruments Co., Tokyo, Japan]), macula, and optic disc (fundus camera CR6-45NM; Canon, Inc., Ota, Tokyo, Japan).

The SFCT was measured by using a spectral-domain OCT (SD-OCT) (wavelength: 870 nm, Spectralis; Heidelberg Engineering Co., Heidelberg, Germany) with EDI modality after pupil dilation.\textsuperscript{17} Seven sections, each comprising 100 averaged scans, were obtained in an angle of 5° to 30° rectangle centered onto the fovea. The horizontal section running through the center of the fovea was selected for further analysis. The SFCT was defined as the vertical distance from the hyperreflective line of the Bruch’s membrane to the hyperreflective line of the inner surface of the sclera. The measurements were performed by using the Heidelberg Eye Explorer software (version 5.3.3.0; Heidelberg Engineering Co.). Only the right eye of each study participant was assessed.

For the calculation of a formula to estimate the CSFP, we used the lumbar CSFP measurements obtained in a previous study on 74 Han Chinese patients who consecutively underwent lumbar puncture for diagnosis and treatment of neurologic diseases.\textsuperscript{13} These included peripheral neuropathy, intracranial hypertension, spontaneous intracranial hypotension, cavernous sinus syndrome, meningitis, multiple sclerosis, unilateral ischemic optic neuropathy, unilateral optic neuritis, optic nerve atrophy, and head injury. The mean measured CSFP was 12.6 ± 4.8 mm Hg. Of the total group, we randomly formed a training group consisting of 32 patients, and a test group including the remaining 42 patients. A multivariate analysis in the training group showed that CSFP was best described by the following formula: CSFP (mm Hg) = 0.44 × Body Mass Index (kg/m\(^2\)) + 0.16 × Diastolic Blood Pressure (mm Hg) − 0.18 × Age (years) − 1.91. The association between higher CSFP and younger age, higher body mass index and higher blood pressure had also been found in other investigations.\textsuperscript{18,19} We then applied the formula in the test group. In the latter, the measured lumbar CSFP (12.6 ± 4.8 mm Hg) did not differ significantly (P = 0.29) from the calculated CSFP (13.3 ± 3.2 mm Hg). The Durbin-Watson value was 2.08. Values falling into the acceptable range of 1.5 to 2.5 indicate a nonsignificant autocorrelation for the residuals in the multiple regression models.\textsuperscript{20} The intraclass correlation coefficient was 0.71. The Bland-Altman analysis revealed that 40 of 42 measurements were within the 95% limits of agreement. If the test group was taken as training group, the algorithm to calculate the CSFP was as follows: CSFP (mm Hg) = 0.85 × Body Mass Index (kg/m\(^2\)) + 0.27 × Diastolic Blood Pressure (mm Hg) − 0.08 × Age (years) − 24.8.

Exclusions for the present study were opacities of the optic media such as cataract, which prevented OCT imaging of the choroid, and insufficient quality of the OCT images for a reliable determination of the SFCT.

Statistical analysis was performed by using a commercially available statistical software package (SPSS for Windows, version 21.0; IBM-SPSS, Chicago, IL). In a first step, we examined the mean values (presented as mean ± standard deviation) of SFCT and CSFP. In a second step, we performed a univariate linear regression analysis with SFCT or CSFP as dependent parameter, and ocular and general parameters as independent parameters. In a third step, we performed a multivariate linear regression analysis with SFCT or CSFP as dependent parameter, and all those parameters as independent parameters that were significantly associated with SFCT in univariate analysis. We presented the 95% confidence intervals (CIs). All P values were two sided and were considered statistically significant when the values were less than 0.05.

**RESULTS**

For the 3468 participants, SFCT measurements and data on body mass index and blood pressure were available for 3230 (93.1%) subjects (1815 [56.2%] women). The group of subjects without complete data on measurements of SFCT, body mass index, or blood pressure, as compared with the group of subjects with complete data, was significantly older (69.6 ± 10.9 years vs. 64.3 ± 9.6 years; P < 0.001), had a higher diastolic blood pressure (75.8 ± 15.7 mm Hg vs. 69.7 ± 12.2 mm Hg; P < 0.001), was more myopic (−1.72 ± 4.60 dipters [D] vs. −0.17 ± 1.96 D; P = 0.001), and had a longer axial length (23.6 ± 1.8 mm vs. 23.2 ± 1.1 mm; P = 0.03). Both groups did not vary significantly in sex (P = 0.08) and body mass index (P = 0.58). The mean calculated CSFP in the group of subjects with SFCT measurements (8.8 ± 3.7 mm Hg) and the group of excluded subjects without SFCT measurements (8.2 ± 4.3 mm Hg) did not differ significantly (P = 0.08). Reasons why SD-OCT images for the measurement of the SFCT were not available in 238 subjects were opacities of the optic media, such as cataract in approximately 90 subjects, and insufficient quality of the images for a reliable determination of the SFCT in approximately 148 subjects.

The mean age in the population of the present study was 64.3 ± 9.6 years (median: 65 years; range, 50 to 93 years), the mean refractive error (spherical equivalent) was −0.17 ± 1.96 D (median: 0.25 D; range: −20.0 to +7.00 D), and mean axial length was 23.2 ± 1.1 mm (median: 23.13 mm; range: 18.96–
TABLE 1. Associations Between Subfoveal Choroidal Thickness and Systemic and Ocular Parameters (Univariate Analysis)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P Value</th>
<th>Standardized Regression Coefficient β</th>
<th>Regression Coefficient B</th>
<th>95% Confidence Intervals of B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated cerebrospinal fluid pressure, mm Hg</td>
<td>&lt;0.001</td>
<td>0.32</td>
<td>9.19</td>
<td>8.25, 10.1</td>
</tr>
<tr>
<td>Age, y</td>
<td>&lt;0.001</td>
<td>−0.44</td>
<td>−4.86</td>
<td>−5.20, −4.51</td>
</tr>
<tr>
<td>Sex, men/women</td>
<td>0.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban/rural region of habitation</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td>0.20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body height, cm</td>
<td>&lt;0.001</td>
<td>0.09</td>
<td>1.14</td>
<td>0.69, 1.59</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>&lt;0.001</td>
<td>0.12</td>
<td>1.14</td>
<td>0.85, 1.46</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>&lt;0.001</td>
<td>0.09</td>
<td>2.45</td>
<td>1.49, 3.41</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>&lt;0.001</td>
<td>0.15</td>
<td>1.28</td>
<td>0.98, 1.58</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>0.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>0.95</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood glucose concentration, mM</td>
<td>0.01</td>
<td>0.05</td>
<td>3.47</td>
<td>0.79, 6.16</td>
</tr>
<tr>
<td>Blood cholesterol concentration, mM</td>
<td>0.03</td>
<td>0.04</td>
<td>4.03</td>
<td>0.39, 7.66</td>
</tr>
<tr>
<td>Blood concentration of high-density lipoproteins, mM</td>
<td>0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood concentration of low-density lipoproteins, mM</td>
<td>0.052</td>
<td>0.04</td>
<td>4.63</td>
<td>−0.04, 9.30</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>&lt;0.001</td>
<td>−0.35</td>
<td>−5.38</td>
<td>−37.0, −30.6</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>&lt;0.001</td>
<td>−0.29</td>
<td>15.6</td>
<td>13.8, 17.5</td>
</tr>
<tr>
<td>Anterior corneal curvature radius, mm</td>
<td>&lt;0.001</td>
<td>−0.10</td>
<td>−4.53</td>
<td>−58.1, −28.4</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>&lt;0.001</td>
<td>−0.09</td>
<td>−19.3</td>
<td>−27.0, −11.6</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>&lt;0.001</td>
<td>−0.07</td>
<td>−21.2</td>
<td>−32.7, −9.7</td>
</tr>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td>&lt;0.001</td>
<td>0.07</td>
<td>2.59</td>
<td>1.24, 3.95</td>
</tr>
</tbody>
</table>

30.88 mm). This study group was almost identical to the group examined in previous investigations on the SFCT without taking into account the CSFP.16

Mean calculated CSFP was 8.8 ± 3.7 mm Hg (median: 8.8 mm Hg) and mean SFCT was 254 ± 107 μm (median: 252 μm; range: 8–854 μm).

In univariate analysis, SFCT was significantly (all P < 0.05) associated with higher CSFP (Fig.), younger age, male sex, urban region, taller body height, higher body weight, higher body mass index, longer waist circumference, higher diastolic blood pressure, and higher blood concentration of glucose and cholesterol, and with the ocular parameters of shorter axial length, refraction error, steeper anterior corneal curvature, flatter anterior chamber depth, thinner lens, and higher intraocular pressure (Table 1). The univariate analysis of the association between SFCT and CSFP showed that for each mm Hg increase in CSFP, the SFCT increased by 9.2 μm (95% CI: 8.3, 10.1) (Fig.). The SFCT was not significantly (all P > 0.20) associated with systolic blood pressure, higher pulse, level of education, and blood concentration of high-density lipoproteins (Table 1).

In a first step of the multivariate analysis, we adjusted the SFCT for those parameters for which the value of the regression coefficient was higher than 0.20 (i.e., age, axial length, region of habitation, CSFP), and for body mass index as parameter combining body height and body weight. It revealed that SFCT remained significantly associated with higher CSFP (P = 0.005), younger age (P < 0.001), shorter axial length (P < 0.001), and lower body mass index (P = 0.03), while region of habitation was no longer significantly associated (P = 0.56). We then included the remaining ocular variables into the list of independent parameters. We dropped intraocular pressure, since it was no longer significantly associated with CSFP (P = 0.35), we dropped anterior chamber depth owing to an inflation variance factor of 2.1 (indicating a high collinearity), and we dropped lens thickness. We arrived at a model in which SFCT was significantly associated with higher CSFP after adjusting for lower age, shorter axial length, lower body mass index, and higher corneal curvature radius (Table 2). If age was dropped, since age was included in the formula to calculate CSFP, SFCT was associated with higher CSFP, shorter axial length, lower body mass index, and longer corneal curvature radius.

The calculated CSFP showed a Gaussian distribution curve (Kolmogorov-Smirnov test; P = 0.75). In multivariate analysis, as also shown in a previous study,21 CSFP was significantly (all P < 0.005) associated with urban region, higher blood concentrations of glucose and triglycerides, higher intraocular pressure, and thinner lens. Adding SFCT showed that CSFP was significantly associated with thicker SFCT (P < 0.001) after adjusting for the region of habitation, higher levels of glucose and triglycerides, higher intraocular pressure, and thinner lens (Table 3).

If we took the second algorithm for calculation of the CSFP (CSFP [mm Hg] = 0.85 × Body Mass Index [kg/m²] + 0.27 × Diastolic Blood Pressure [mm Hg] − 0.08 × Age [years] − 24.8), similar results were obtained: SFCT was significantly associated with higher CSFP (P = 0.009) after adjusting for lower age, shorter axial length, lower body mass index, and higher corneal curvature radius (Table 2). If age was dropped, since age was included in the formula to calculate CSFP, the SFCT was associated with higher CSFP, shorter axial length, lower body mass index, and longer corneal curvature radius (Table 2).

**DISCUSSION**

Using data of body mass index, diastolic blood pressure, and age for the estimation of CSFP, our population-based study showed that the subfoveal choroid in a general population was associated with a higher CSFP. After adjustment for younger age, shorter axial length, lower body mass index, and higher corneal curvature radius, SFCT increased significantly with higher CSFP. In univariate analysis, SFCT increased by 9.2 μm for each mm Hg increase in CSFP. In a reverse manner, CSFP was significantly associated with thicker SFCT after adjusting for the region of habitation, blood concentrations of glucose and triglycerides, intraocular pressure, and lens thickness.

In the univariate analysis, both SFCT and CSFP were significantly associated with younger age. The relationship
between thicker choroid and younger age, as also shown in other studies,22,25 may perhaps be explained by an age-related loss in choroidal tissue. The relationship between higher estimated CSFP and younger age, as also found in other studies, may be parallel to the age-related decline in intraocular pressure.18,26 Interestingly, SFCT was significantly (P < 0.001) associated with diastolic blood pressure but not significantly (P = 0.61) with systolic blood pressure, while CSFP was significantly associated with both blood pressure parameters. While the reasons for this discrepancy have not fully been explored yet, one may speculate that the more marked and the more rapid changes in systolic blood pressure are reflected faster in changes in CSFP while SFCT may react more slowly and may thus be influenced mainly or only by the diastolic blood pressure value.

These findings fit with clinical studies on circadian variations in SFCT, since the CSFP shows profound circadian changes due to the hydrostatic differences between the supine position and the sitting or standing position. Chakraborty and colleagues27 have investigated the pattern of diurnal variations in choroidal thickness and other ocular biometric parameters during 2 consecutive days. These authors have found that the choroid is thicker at night and thinnest in the morning, with a mean amplitude of change in choroidal thickness of 29 μm. Usui and colleagues28 have examined 38 eyes of 19 healthy volunteers and measured the SFCT every 3 hours over a 24-hour period. They have found that the SFCT is thickest (291 ± 111 μm) at 3 AM in the early morning, and that it is thinnest at 6 PM (272 ± 104 μm). In 32 of 38 eyes, the SFCT was thickest between 3 AM and 9 AM, and it was thinnest between 3 PM and 9 PM in 27 of 38 eyes. In an investigation by Tan et al.,29 12 healthy volunteers underwent sequential ocular imaging on 2 separate days at five fixed, 2-hour time intervals, starting at 9 AM. They have observed a characteristic diurnal pattern in choroidal thickness, with the highest mean choroid thickness detected at 9:00 AM (the earliest measurement point) with a mean SFCT of 372 μm and a continuous decrease in SFCT over the subsequent time points to a low of 340 μm at 6 PM. These diurnal changes in the SFCT are usually accompanied by opposed changes in axial length. Accordingly, previous studies have shown an increase in optical axial length in the morning and a decrease in the evening.30 In a similar manner, experimental studies have revealed circadian rhythms in axial length, choroidal thickness, and intraocular pressure, for example, in chickens and in primates such as the common marmoset. Nickla and colleagues31 have examined 14 marmosets by tonometry and high-frequency A-scan ultrasonography to measure the ocular dimensions. The authors have observed

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P Value</th>
<th>Standardized Regression Coefficient β</th>
<th>Regression Coefficient B</th>
<th>95% Confidence Intervals of B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subfoveal choroidal thickness, μm</td>
<td>&lt;0.001</td>
<td>0.21</td>
<td>0.007</td>
<td>0.006, 0.009</td>
</tr>
<tr>
<td>Rural/urban region of habitation</td>
<td>&lt;0.001</td>
<td>−0.31</td>
<td>−2.32</td>
<td>−2.60, −2.04</td>
</tr>
<tr>
<td>Blood glucose concentration, mM</td>
<td>0.02</td>
<td>0.04</td>
<td>0.10</td>
<td>0.02, 0.19</td>
</tr>
<tr>
<td>Blood triglyceride concentration, mM</td>
<td>&lt;0.001</td>
<td>0.09</td>
<td>0.13</td>
<td>0.07, 0.18</td>
</tr>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td>&lt;0.001</td>
<td>0.12</td>
<td>0.17</td>
<td>0.12, 0.22</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>&lt;0.001</td>
<td>−0.22</td>
<td>−2.39</td>
<td>−2.79, −1.99</td>
</tr>
</tbody>
</table>

Table 3. Associations Between Estimated Cerebrospinal Fluid Pressure (mm Hg) and Systemic and Ocular Parameters (Multivariate Analysis)
that the choroid thickens during the night and thins during the day at all ages measured.

Interestingly, the amount of macular edema in patients showed similar diurnal changes as described for choroidal thickness. Paques and colleagues have examined patients with macular edema due to central retinal vein occlusion and observed a significantly thicker macular edema at 7 AM than at 7 PM, parallel to changes in visual acuity. Similar observations have been reported by Gupta et al. These findings pointing to an increased pressure in the central retinal vein in the morning as compared to the evening may be explained by the assumption that the pressure in the central retinal vein depends on the CSFP, since the vein passes through the optic nerve cerebrospinal fluid space and drains into the intracranial cavernous sinus. Both findings, the diurnal changes in the SFCT and the diurnal changes in the amount of macular edema, suggest the CSFP may play a role in the physiology of the eye, in particular for the pressure and thus the thickness of the choroid, as well as for the pressure in the central retinal vein.

In a previous study, the reproducibility of the SFCT measurements has been tested by comparing the SFCT measurements obtained by grader 1 and by grader 2. The mean difference between both measurements is $3.14 \pm 13.1$ μm (95% CI: 0.0, 24.0), and the Bland-Altman plot shows that 1.9% (61/3233) of the points are located outside the 95% limits of agreement. For the assessment of the intra-observer reproducibility, 21 eyes of 21 healthy subjects were scanned 10 times with 1-minute breaks between each examination. The intraclass coefficient was 1.00 and the mean coefficient of variation was 0.85% ± 1.48%. The results of the present investigation on the use of the CSFP formula with respect to the SFCT in the Beijing Eye Study correspond with those of a recent study on the population of the Central India Eye and Medical Study in which the translamina cribrosa pressure difference was determined on the basis of the same CSFP formula as in the present study. In the Central India Eye and Medical Study, the translamina cribrosa pressure difference, but not intraocular pressure, is significantly associated with open-angle glaucoma but not with angle-closure glaucoma, while the intraocular pressure, but not the translamina cribrosa pressure difference, is significantly associated with angle-closure glaucoma but not with open-closure glaucoma.

A major assumption of this article was that CSFP can be assessed by a formula based on the three parameters of diastolic blood pressure, age, and body mass index. This formula was arrived at by using data from an observational study on patients undergoing lumbar puncture for neurologic diseases, which eventually were not felt to have influenced the CSFP. Since inclusion of invasive lumbar CSFP measurements into the design of a population-based study is not acceptable, one may plan for a prospective study in which the association between SFCT and CSFP is directly tested. In such an investigation, diurnal measurements of diastolic blood pressure could be compared with diurnal measurements of SFCT, or the association between SFCT and CSFP could be addressed by examining subjects at different body postures (with different CSFPs). The question may arise, however, whether an association between relatively small diurnal changes in SFCT, or posture-dependent changes in SFCT, and corresponding changes in diastolic blood pressure (the two other determinants in the CSFP formula, i.e., age and body mass index, are constant) can be found. One may also take into account that blood pressure can show rapid changes, while one may assume that the SFCT may change relatively slowly. Another model to assess the postulated association between SFCT and CSFP may be a condition with chronically elevated CSFP such as in idiopathic intracranial hypertension. In such a study, patients would undergo OCT for measurement of the SFCT at baseline and again after a therapeutically induced reduction in CSFP. Potential limitations of our study should be mentioned. First, the whole statistical analysis depended on the formula to calculate the CSFP. This formula was developed in a pilot study.

![Figure](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933471/ on 09/23/2017)
that included a relatively small number of subjects. These subjects had a clinical reason to undergo lumbar puncture, so that they were not normal subjects. Although the final neurologic diagnosis made it unlikely that the underlying neurologic condition had influenced the CSFP, one has to keep in mind that the participants were not randomly selected normal subjects. One may also consider that the estimation of CSFP was derived from a multivariate formula incorporating body mass index, diastolic blood pressure, and age. The mathematical result of this formula was termed CSFP. Although this calculated CSFP value was primarily the result of a mathematical equation, it correlated well with invasively measured CSFP values in the independent test group in the pilot study. The unknown general validity of the equation to estimate the CSFP may however be the most important limiting factor of our study. In view of this weakness in the study design, one may however also take into account that it would not have been possible to measure the CSFP in a population-based study. Second, as in any prevalence study, nonparticipation may be a major concern. The Beijing Eye Study 2011 had a reasonable response rate of 78.8%; however, differences between participants and nonparticipants could have led to a selection artifact. Third, blood pressure, as part of the formula to calculate CSFP and the SFCT, was measured only once, so that diurnal and situation-dependent variations may have influenced the measurements and statistical analysis.

Fourth, the participants of our study underwent the OCT examinations at various times of the day. Since these examinations were performed in a randomized manner with respect to when they were performed, it is unlikely that the reported dependence of the choroidal thickness measurement on the time of day introduced a bias into our study. It will have increased the inaccuracy or noise in the measurements, leading to a reduced statistical power of the measured parameters. Despite this weakness, however, the association between the SFCT and CSFP was statistically significant so that this limitation of the study may serve to strengthen the results and conclusions. If we had documented the time of day when the OCT images were taken, we would have had the possibility to assess a change in the SFCT, dependent on the time of day that the OCT images were taken, and to look for a parallel change in the estimated CSFP. Fifth, as with any population-based study, our investigation included all eligible and participating subjects from the study region. Therefore, also patients with diseases, such as disorders of the optic nerve and macula, were included, although these diseases may have affected the choroidal thickness, either in the sense of a thickening or in the sense of a thinning. Future studies may address whether these diseases show a different association between the SFCT and CSFP.

In conclusion, thicker subfoveal choroid was associated with higher CSFP after adjustment for age, axial length, body mass index, and corneal curvature radius. This association may explain thicker SFCT values in the morning than evening. It shows the importance of the CSFP for the physiology of the eye.

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