Does Acute Primary Angle-Closure Cause an Increased Choroidal Thickness?

Wei Wang, Minwen Zhou, Wenbin Huang, Shida Chen, Xiaoyan Ding, and Xiulan Zhang

Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-sen University, Guangzhou, People’s Republic of China

Correspondence: Xiulan Zhang, Professor of Ophthalmology, Vice Director of Glaucoma Department, Director of Clinical Research Center, Director of Institution of Drug Clinical Trials, Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-sen University, 54 S. Xianlie Road, Guangzhou, China 510060; zhangxl2@mail.sysu.edu.cn.

WW and MZ contributed equally to the work presented here and therefore should be regarded as equivalent authors.

Submitted: January 24, 2013
Accepted: April 6, 2013


Acute primary angle-closure (APAC) is a well-known ophthalmic emergency, with typical symptoms and clinical signs, such as sudden onset of ocular discomfort or pain, subjective blurring of vision, and sudden and excessive increases in IOP. Eyes with APAC have important biometric differences compared to healthy eyes, such as a shallower anterior chamber, thicker lens, smaller corneal diameter, anterior lens-iris diaphragm, and shorter axial length.1 Fellow eyes of patients presenting with APAC are at risk of a similar attack because of the similar anatomic structure in both eyes. The predominant mechanism in the development of APAC is increased resistance, which is caused by relative pupillary block preventing the aqueous humor from flowing through the pupil.2 Recent interest has focused on the choroid as an important structure involved in the pathophysiology of APAC.3 If the choroid has an important role in APAC eyes, choroidal thickness may be a crucial clinical measurement indicator. Using enhanced depth imaging optical coherence tomography (EDI-OCT) enables visualization and measurement of the choroidal thickness without invasive examination.4–13 Our research group has studied the choroidal thickness in normal Chinese subjects14 and in the fellow eyes of APAC patients using this technique.

In our study, we focused on the choroidal thickness in APAC eyes. When an eye suffers an APAC attack, the EDI-OCT is affected by the opacity of the refractive media, and it is not possible to obtain a clear image. Thus, only patients whose IOP had decreased, and where the optical media had cleared following treatment with adjunctive glaucoma medications or anterior chamber paracentesis were enrolled in the study. The choroidal thickness of the APAC eyes was compared to that of fellow eyes meeting a diagnosis of primary angle-closure suspect (PACS).

METHODS

Subjects and Enrollment Criteria

This prospective, comparative study was approved by the Ethical Review Committee of Zhongshan Ophthalmic Center, and adhered to the provisions of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all participants involved in the study. All subjects were from a Chinese Han population.

All enrolled glaucoma patients fulfilled the following inclusion criteria: Subjects were >18 years old, one eye had experienced APAC when the IOP was decreased and when the optical media had cleared following treatment with adjunctive glaucoma medications or anterior chamber paracentesis, the fellow eyes diagnosed with PACS had clear ocular media, and a clear image was obtained to enable precise measurement of the choroidal thickness. APAC was defined according to the following criteria:16 Presence of at least two of the following symptoms to ocular or periocular pain, nausea and/or vomiting,
Increased Choroidal Thickness in APAC

A single experienced ophthalmologist masked to the clinical diagnosis of the patient performed the EDI-OCT examinations. Choroidal imaging was performed using a Heidelberg Spectralis instrument (Heidelberg Engineering, Heidelberg, Germany). Choroid imaging was averaged for 100 scans using the device’s automatic averaging and eye-tracking features. For measurements of the macula and the peripapillary choroidal thickness, horizontal and vertical sections going directly through the center of the fovea and the optic disk were selected (Figs. 1, 2). A 360°, 3.4 mm diameter peripapillary circle scan also was performed, using the standard protocol for choroidal thickness assessment (Fig. 2).14 The resultant images were viewed and measured with Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering). Keratometry readings and the most recent refraction were entered into the software program to estimate the optical magnification; therefore, allowing more accurate comparisons across individuals. The choroid was measured from the outer portion of the hyperreflective line corresponding to the RPE of the inner surface of the sclera. The thickness of the retina was measured from the most anterior hyperreflective line, which corresponds to the inner limiting membrane, to the center of the most posterior hyperreflective line, which corresponds to the inner limiting membrane to RPE. Measurements were taken of the subfovea, and at 1 and 3 mm to the fovea superiorly, inferiorly, temporally, and nasally. The choroid was measured by two independent graders who were blinded to the diagnosis. If the difference in the thickness measurements of the two examiners exceeded 15% of the mean of the two values, there was open adjudication with the senior author.15,18 The values of the measurements were compared for each observer and then averaged for analysis. The images were obtained with the best visualization of the border between the choroid and the sclera, known as the choroidal–scleral interface (CSI). If neither image had a clearly identifiable CSI, additional images were viewed to produce the best possible view of the CSI.

The peripapillary choroidal thickness in the superior, inferior, nasal, and temporal quadrants also was measured. Two measurements were taken in each of the four quadrants at 1 mm intervals along the line of the RPE. For example, the first measurement was made close to the optic nerve at 1 mm distal to the beginning of the RPE, and the second measurement was taken 2 mm away from the beginning of the RPE. A peripapillary circle scan was performed, and the retinal and choroidal thicknesses were delineated manually using the Heidelberg Eye Explorer software (introduced above).

The macular and the peripapillary retinal thickness also were measured using the same methods mentioned above.

Statistical Analysis
Based on data from our previous study,15 11 pairs of eyes would be required to detect a significant difference in thickness of at least 81.74 μm between APAC eyes and fellow eyes at a significance level of 0.05 and a power of 0.90, for an SD of 72.37 μm. The data were processed and analyzed statistically using SPSS for Windows XP (Version 13.0; SPSS, Chicago, IL). For the comparison between the two different groups, a paired t-test was used to evaluate differences in the average between the normal distributed data. A Bonferroni adjustment for multiple comparisons was applied to all pairwise comparisons. For the macular choroidal thickness, a
Increased Choroidal Thickness in APAC

**Figure 1.** EDI-OCT scans showing macula choroidal thickness of the same subject. SFCT and 1 mm, 3 mm superior (S) and inferior (I) to the fovea was measured vertically, and 1 mm, 3 mm nasal (N), and temporal (T) to the fovea was measured horizontally from the outer border of the retinal pigment epithelium to the inner border of the sclera.

**Figure 2.** EDI-OCT scans showing peripapillary choroidal thickness of the same subject case as in Figure 1. The choroidal thickness in 1 mm, 2 mm N and T to the optic disc was measured horizontally (*top*), and 1 mm, 3 mm S and I to the optic disc was measured vertically (*second row*). The peripapillary choroidal thickness of all the segments were measured with 360° circle scans. This scan was performed and choroidal thickness was delineated manually using the Heidelberg Eye Explorer software as the area of visible choroidal vasculature between the outer retinal pigment epithelial border and the inner scleral wall (*bottom*).
Increased Choroidal Thickness in APAC

TABLE 1. Demographic and Baseline Characteristics of Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>N patients (N eyes)</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Mean age, y (SD)</td>
<td>60.8 (9.2)</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>6/15</td>
</tr>
<tr>
<td>Laterality of affected eye, right/left</td>
<td>9/12</td>
</tr>
<tr>
<td>Duration of experienced attack, d (SD)</td>
<td>6.5 (2.4)</td>
</tr>
<tr>
<td>Presenting IOP, mm Hg, affected eye (SD)</td>
<td>49.1 (11.4)</td>
</tr>
<tr>
<td>N of glaucoma medications (SD)</td>
<td>4.1 (0.7)</td>
</tr>
<tr>
<td>IOP at imaging, mm Hg (SD)</td>
<td>16.1 (3.7)</td>
</tr>
<tr>
<td>N of patients underwent paracentesis</td>
<td>5</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SD.

P value < 0.005 was considered significant. A P value < 0.008 was considered significant for the choroidal thickness of the peripapillary region. Independent variables for the multivariable regression model with a clustering level at the individual level were chosen using the stepwise selection method, with the criterion for inclusion in the model set at a probability value of 0.10. For all the tests except the macular and peripapillary comparisons, P < 0.05 was considered to be significant.

RESULTS

Demographic and Baseline Characteristics of the Patients

Six patients were excluded because a clear OCT image could not be obtained due to a lack of clarity in the optical media, despite a decrease in the IOP. One case was excluded because the border between the choroid and sclera could not be visualized, although the optical media was clear. Finally, 21 Chinese patients (21 pairs of eyes) with unilateral APAC and fellow eyes defined as PACS with high-quality OCT images were analyzed. The mean age of the patients was 57.7 years (SD ± 11.3 years, range 38–78 years). The study included 15 females and six males. The mean number of days that the patients had experienced APAC in one eye was 6.5 (SD ± 2.4 days, range 3–9 days). The demographic and baseline characteristics of the patients are summarized in Table 1.

The mean spherical equivalent was 0.6 D (SD ± 1.4 D) in the APAC eyes and 1.0 (SD ± 1.3 D) in the PACS eyes. The mean axial lengths of the APAC and PACS eyes were 22.3 mm (SD ± 0.9 mm) and 22.2 mm (SD ± 0.9 mm), respectively. All data are summarized in Table 2. There were no significant differences in any of the variables between the two groups.

Choroidal Thickness in the Macular Region

The mean macular choroidal thickness was greatest at the subfovea for both groups. It decreased in vertical and horizontal sections, and reached a minimum of 3 mm from the fovea. The mean subfoveal choroidal thickness was 349.0 μm (SD ± 78.1) in the APAC eyes and 308.1 μm (SD ± 70.5) in the PACS eyes, with a statistically significant difference (P < 0.05). The nasal choroidal thickness was thinnest, and the superior choroidal thickness was thickest in all quadrants. Table 3 shows the mean choroidal thickness at each macular location in both groups. The macular choroidal thickness was significantly greater in the APAC eyes than in the PACS eyes at all locations except at 1 mm, 3 mm superior, 3 mm inferior, and 3 mm temporal from the fovea (P < 0.005). The mean choroidal thickness was plotted for each location, measured along the horizontal and vertical sections (Fig. 3). The subfoveal choroidal thicknesses (SFTCs) of all the subjects are shown in Figure 4.

Choroidal Thickness in the Peripapillary Region

With Line Scans

The peripapillary choroidal thickness in both groups is shown in Table 4. The peripapillary choroidal thickness at all locations in the APAC eyes was greater than that in the PACS eyes; however, none of the locations reached statistical significance. In the horizontal and vertical sections, both groups showed comparable trends, with the choroidal thickness being thinnest in the inferior peripapillary region and increasing moving distally from the optic disc.

Choroidal Thickness in the Peripapillary Region

With 360° Circle Scans

With the 360° circle scans, the peripapillary choroidal thickness of all segments in the APAC eyes was greater than that in the PACS eyes, but neither reached statistical
significance (all P > 0.05). In both groups, the choroidal thickness of the inferior segment was the thinnest of all segments. Table 5 shows the average choroidal thickness of the peripapillary segment in both groups with the circle scans.

Retinal Thickness in the Macular and the Peripapillary Region

The mean retinal thickness was smallest at the fovea for both groups. Compared to the PACS eyes, the APAC eyes showed no statistically significant difference in the retinal thickness at any macular or peripapillary location or segment (all P > 0.05).

Stepwise Multiple Regression Analysis

We performed stepwise analysis to determine factors associated with the subfoveal choroidal thickness. The model was fitted with the diagnosis, age, and diastolic blood pressure variables. An APAC diagnosis (APAC eyes with a subfoveal choroidal thickness that was, on average, 39.7 μm thicker than that of the PACS eyes), age, and diastolic blood pressure were associated commonly with the subfoveal macular choroidal thickness (all P < 0.05). There was no association between the

![Graph showing the mean subfoveal choroidal thickness, and 1 mm, 3 mm N, and T to the fovea (top), the mean subfoveal choroidal thickness, and 1 mm, 3 mm S, and I to the fovea (bottom).](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933469/)

*Statistically significant difference.*

![The subfoveal choroidal thicknesses are shown of all subjects. F, fellow eyes (PACS eyes); A, APAC eyes.](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933469/)

**Figure 3.** Graph showing the mean subfoveal choroidal thickness, and 1 mm, 3 mm N, and T to the fovea (top), the mean subfoveal choroidal thickness, and 1 mm, 3 mm S, and I to the fovea (bottom). The choroid thickness of the APAC eyes was significantly greater than that of the PACS eyes at most locations. *Statistically significant difference.*

**Figure 4.** The subfoveal choroidal thicknesses are shown of all subjects. F, fellow eyes (PACS eyes); A, APAC eyes.
Table 4. Average Choroidal Thickness and 95% CI at Different Locations in Peripapillary Area With Line Scans

<table>
<thead>
<tr>
<th>Location, mm From Optic Disc</th>
<th>Affected Eyes, APAC, µm</th>
<th>Fellow Eyes, PACS, µm</th>
<th>95% CI, µm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>S1 mm</td>
<td>198.4</td>
<td>60.9</td>
<td>191.3</td>
</tr>
<tr>
<td>S2 mm</td>
<td>242.1</td>
<td>71.1</td>
<td>226.2</td>
</tr>
<tr>
<td>I1 mm</td>
<td>178.6</td>
<td>61.0</td>
<td>165.0</td>
</tr>
<tr>
<td>I2 mm</td>
<td>195.0</td>
<td>64.8</td>
<td>183.6</td>
</tr>
<tr>
<td>N1 mm</td>
<td>219.3</td>
<td>65.3</td>
<td>193.2</td>
</tr>
<tr>
<td>N2 mm</td>
<td>256.5</td>
<td>69.5</td>
<td>230.4</td>
</tr>
<tr>
<td>T1 mm</td>
<td>204.8</td>
<td>54.5</td>
<td>190.5</td>
</tr>
<tr>
<td>T2 mm</td>
<td>205.1</td>
<td>52.4</td>
<td>204.8</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SD.  
* PACS group as reference.  
† Paired t-test.

Δ SFCT and the number of days after the attack (β = 0.72, P = 0.870).

DISCUSSION

In our study, using EDI-OCT, we investigated the choroidal thickness of APAC eyes within the macula and peripapillary regions by comparing the measured values with those of the fellow eyes. To the best of our knowledge, this is the first time that high-quality imaging modalities have been used to compare the choroidal thickness between APAC eyes and the fellow eyes. The study found that the APAC eyes demonstrated an average subfoveal choroidal thickness of 349.0 µm (SD ± 78.1), whereas the fellow eyes had an average thickness of 380.1 µm (SD ± 70.5). We first showed that the mean SFCT was significantly greater in the APAC eyes than in the fellow eyes. More importantly, unlike other studies, we set strict recruitment and exclusion criteria in our study. Our data are highly comparable in terms of the patients recruited, with the demographic and baseline characteristics of the groups closely matched. Based on the data, we concluded that the macular choroidal thickness in APAC eyes is greater than in fellow eyes.

As is well known, fellow eyes of patients presenting with APAC are at risk of a similar attack developing because of the similar anatomic structure in both eyes. 21 We examined demographic and baseline characteristics of the groups closely matched. Based on the data, we concluded that the macular choroidal thickness in APAC eyes is greater than in fellow eyes. More importantly, unlike other studies, we set strict recruitment and exclusion criteria in our study. Our data are highly comparable in terms of the patients recruited, with the demographic and baseline characteristics of the groups closely matched. Based on the data, we concluded that the macular choroidal thickness in APAC eyes is greater than in fellow eyes.

In our study, we should be conscious that the choroidal thickness in all the APAC eyes was measured when the IOP decreased from an extraordinary high IOP mean of 49.1 ± 11.4 mm Hg to a mean of 16.1 ± 3.7 mm Hg. As is well known, the choroid is a highly vascular structure, which has one of the highest ratios of blood flow to tissue volume in the body. 22 We speculated that the sudden decrease in the IOP may have caused choroidal hypertransfusion and that the engorgement of the choroidal vessels may have a role in the greater choroidal thickness. A previous study found that in eyes suspected of having PAC, an acute increase in IOP accompanies choroidal thinning, 23 thereby indirectly confirming our hypothesis.

The finding of greater macular choroidal thickness in the APAC eyes compared to the fellow eyes is novel and has not been reported previously to our knowledge. The fellow eyes showed a greater level of choroidal thickness compared to normal subjects in our previous study and in another study. 15, 24 However, we cannot fully explain the reason for this observation. The increase in the choroidal thickness noted in

Table 5. Average Choroidal Thickness and 95% CI at Different Segment With 360° Peripapillary Circle Scans

<table>
<thead>
<tr>
<th>Sector</th>
<th>Affected Eyes, APAC, µm</th>
<th>Fellow Eyes, PACS, µm</th>
<th>95% CI, µm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>S</td>
<td>201.8</td>
<td>51.5</td>
<td>188.2</td>
</tr>
<tr>
<td>ST</td>
<td>198.5</td>
<td>53.1</td>
<td>188.8</td>
</tr>
<tr>
<td>SN</td>
<td>205.1</td>
<td>52.4</td>
<td>187.7</td>
</tr>
<tr>
<td>I</td>
<td>170.9</td>
<td>55.6</td>
<td>148.6</td>
</tr>
<tr>
<td>IT</td>
<td>172.2</td>
<td>58.0</td>
<td>148.2</td>
</tr>
<tr>
<td>IN</td>
<td>169.5</td>
<td>55.3</td>
<td>149.6</td>
</tr>
<tr>
<td>T</td>
<td>198.8</td>
<td>56.5</td>
<td>176.8</td>
</tr>
<tr>
<td>N</td>
<td>191.8</td>
<td>58.0</td>
<td>172.2</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SD. ST, superotemporal; SN, superonasal; IT, inferotemporal; IN, inferonasal.  
* PACS group as reference.  
† Paired t-test.
the APAC and fellow eyes suggested that it essentially may be a bilateral genetic disorder. In addition to the shallow anterior chamber, shorter axial length, small corneal diameter, radius of curvature, and increased LT, the increased choroidal thickness might be another anatomic characteristic of APAC and fellow eyes. A greater choroidal thickness might be associated with a higher incidence of acute attacks. However, we feel that a more extensive, population-based study, for example, is needed to conform or to refute this finding. More useful information might be gained by capturing EDI-OCT images of patients before they experience an attack of APAC in a population-based study and subsequent images when these patients suffer the attack and after the attack (when the IOP is decreased).

Uveal effusion might be another potential source of the greater choroidal thickness in APAC eyes. A prospective, consecutive case series study of APAC and unaffected fellow eyes found that uveal effusion diagnosed by UBM is prevalent in APAC. Inflammation, hypotony, sudden IOP reduction, and/or drug therapy with acetazolamide may contribute to the prevalence of uveal effusion in APAC eyes. However, that study was unable to show changes in the posterior choroid or to measure the choroidal thickness because of the limitation of UBM. The use of EDI-OCT could compensate for this limitation, making it possible to examine the overall posterior polar choroid with 6 mm diameter. We found that the choroidal thickness in the macular region in the APAC eyes was thicker at all locations compared to the fellow eyes, indicating that the choroid is thickened diffusely. It is likely that the greater choroidal thickness may be related to uveal effusion. In fact, Harada et al. found that idiopathic uveal effusion syndrome could be detected by EDI-OCT.

The hypothesis of Quigley et al. also may explain partly this phenomenon. According to this hypothesis, choroidal expansion has an important role in APAC. The choroidal expansion might be present before and contribute to the greater choroidal thickness in APAC. The expansion may be due to an increase in the volume of the extravascular choroid space. In other words, an increase in the choroidal volume would increase the IOP coincident with the expansion. Then, aqueous humor leaves the anterior chamber, a pressure differential would develop between the vitreous cavity and the posterior chamber, on the one hand, and the anterior chamber, on the other. This may worsen the pupil block. If the thickening choroid is the result of choroidal expansion, the question is whether the choroidal thickness continues to expand over time and at what point it returns to a thinner choroid, more like that in the fellow eye. Repeated measurements of the choroidal thickness after the IOP has decreased might help us to understand the choroidal expansion more clearly.

Antiglaucoma eye drops are another important factor that might influence the choroidal thickness. In our study, most of the APAC eyes had received such drops, but the fellow eyes had not. These eye drops potentially may have resulted in the change in the choroidal structure. Several studies have proven that some antiglaucoma agents, such as topical alpha-2 agonists, acetazolamide, and dorzolamide, can increase the choroidal blood flow. In the multivariable regression model, we found that age and diastolic blood pressure also were associated with the choroidal thickness, but not with the axial length as reported in other studies. The relatively small sample size may explain this discordance. Interestingly, in our study, diastolic blood pressure was associated independently with the choroidal thickness. Not enough literature studies had reported such an association previously. Further research is required to shed light on this issue.

Our study has some limitations. First, the measurements of the choroidal thickness were performed manually, and automated software will be required for a more objective evaluation. Second, the sample size was limited. However, the study enrolled 21 pairs of eyes, and it was estimated that 11 pairs were sufficient to draw a significant difference, with a 90% power. When considering the relative sample size, we believe that the strict inclusion criteria for patients, and the close matching of the APAC and PACS eyes should be taken into account. Third, in our assumptions and speculations, we considered the change in the posterior choroid to be a general change that was distributed proportionately throughout the choroid. However, it is possible that only segmental changes in the choroidal thickness occurred. Further research is required to elucidate these issues.

CONCLUSION

In conclusion, the choroidal thickness in the macular region was greater in the APAC eyes than in the PACS eyes when the IOP was reduced. Unfortunately, we still may not conclude that the choroidal thickening was present before or during the attack. Thus, the source of this difference remains unclear.

Acknowledgments

Supported by the National Natural Science Foundation of China (81170849), the Doctoral Program of Higher Education of China (RFDP 201000171110077), and the Fundamental Research Funds of State Key Laboratory of Ophthalmology (2011C02). The authors alone are responsible for the content and writing of the paper.

Disclosure: W. Wang, None; M. Zhou, None; W. Huang, None; S. Chen, None; X. Ding, None; X. Zhang, None

References


