Ultrasonographic Biomicroscopy, Scheimpflug Photography, and Novel Provocative Tests in Contralateral Eyes of Chinese Patients Initially Seen With Acute Angle Closure

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**Objectives:** To compare ocular biometry of the contralateral eyes of individuals seen with acute angle closure (AAC) with eyes of population-based control subjects, and to assess novel provocative tests to study the mechanism of AAC.

**Design:** Prospective case-control study.

**Participants:** Chinese persons seen as incident cases of AAC and Chinese population-based controls.

**Methods:** Slitlamp assessment, ultrasonographic biomicroscopy, Scheimpflug photography, and provocative testing were performed.

**Main Outcome Measures:** Ocular biometric parameters including anterior chamber depth, limbal anterior chamber depth, axial length, lens thickness, and radius of corneal curvature were obtained. Ultrasonographic biomicroscopy parameters that include the angle-opening distance at 500 µm and the angle-recess area were noted. Scheimpflug photography produced a single measure of angle width.

**Results:** Contralateral eyes of cases of AAC had shorter axial lengths, shallower anterior chamber depths, thicker lenses, and steeper radii of corneal curvature ($P<.01$). After adjusting for age and sex, cases had a mean adjusted axial length that was 1.2 mm shorter, an optical anterior chamber depth that was 0.63 mm shallower (24% shallower than controls), and lenses that were, on average, 0.35 mm thicker ($P<.01$). Furthermore, using multiple logistic regression to adjust for age and sex, patients with primary angle-closure glaucoma were 19 times as likely to have a shallower limbal anterior chamber depth (25%; 95% confidence interval, 8.3-45.2). Adjusting for age and sex, the mean angle-opening distance at 500 µm was 0.14 U less for cases, with a mean of 0.26 U in controls, making the angle-opening distance at 500 µm, on average, 54% less among cases. Scheimpflug photographs revealed an adjusted angle width of 21.6° for controls and 15.1° for cases ($P<.05$). Dynamic testing showed that the angle of control eyes tended to shallow less when going from light to dark and tended to open more when given 1 drop of pilocarpine hydrochloride.

**Conclusions:** Contralateral eyes of individuals having an AAC attack tend to be shorter and have more crowded anterior segments than those of healthy controls. These static measures of ocular biometry indicate why some individuals are predisposed to AAC. Dynamic measures of the response to luminance changes and pilocarpine therapy indicate that differential reactions to these stimuli are also associated with an AAC attack.

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Primary angle-closure glaucoma (PACG) is a leading cause of world blindness, with higher rates documented in Asian populations. Chinese subjects in Singapore and a southern Indian population both had high rates of PACG in recent population-based studies, with about 1% of the individuals older than 40 years having PACG. The rates of visual impairment and blindness from PACG are likely 2 to 3 times those of open-angle glaucoma. Given that almost half of the world’s population lives in China and India, millions of individuals are at risk of PACG. Acute angle closure (AAC) accounts for about 20% of PACG and frequently results in severe vision loss. Singapore has one of the highest rates of AAC in the world with an islandwide incidence estimated at 12.2/100000 per year in the population older than 30 years. Incidence increases with age and is more common among women, with an incidence of 68.5/100000 per year among Chinese women older than 60 years. Acute angle closure is likely to increase over the coming decades as the populations of these countries age. It is anticipated that mainland China alone will have 631 million people older than 50 years in 2050.
Previous research on risk factors for primary angle closure (PAC) has frequently studied heterogeneous populations including individuals who have had AAC attacks, those with intermittent symptoms of angle closure, and still others with chronic angle closure. Those studies, mostly in Inuit and European-derived white populations, have looked for anatomical and some dynamic or physiological factors that predispose individuals toward PAC.10 11 The major ocular anatomical risk factors include an anteriorly positioned and proportionally thicker lens, both of which contribute to shallow anterior chamber depth (ACD). Recent studies in Chinese populations in Singapore and Taiwan have supported these findings.1,5,12

While several studies have found the mean ACD to be lower among populations with high rates of PACG,13-14 a recent study found no difference between Taiwanese Chinese and European-derived whites from East Baltimore, Md.15 If the mean ACD is, indeed, similar across populations, then the higher rates of PACG among Chinese individuals may be caused by unexplained differences in the anterior chamber angle anatomy or dynamic factors of the eye that predispose Chinese individuals to AAC attacks.

This study was undertaken to compare prospectively individuals having AAC attacks with population-based control subjects. Detailed biometric examination of the symptomatic eye is difficult because of disturbed physiology and antecedent treatment. The contralateral eye, however, probably represents a preattack state. We, therefore, studied the contralateral eyes of individuals having a monocular AAC attack. These eyes are at high risk of developing AAC if left untreated.16-18 In addition to comparing traditional biometric parameters, the status of the anterior chamber angle was assessed by ultrasonographic biomicroscopy and Scheimpflug photography. Furthermore, tests of dynamic changes in the anterior segment in response to external stimuli were conducted in both cases of AAC and controls.

METHODS

All individuals having AAC initially seen at the Singapore National Eye Centre, Singapore, from March 15, 1999, through July 20, 2001, were invited to participate in the study. Controls were recruited from subjects of an eye disease prevalence survey conducted between January 6, 1997, and September 4, 1998. All participants in this study gave written, informed consent in accord with the Johns Hopkins University institutional review board, the Singapore National Eye Center Ethics Review Board, and the Declarations of Helsinki.

CASE DEFINITION AND SELECTION

All cases of AAC initially seen at the Singapore National Eye Centre were potentially eligible for the study. Patients with AAC had to have at least one of the following symptoms in association with an occludable angle (no trabecular meshwork visible for at least 270°) and an intraocular pressure of greater than 25 mm Hg; sudden onset of ocular discomfort or pain, nausea, and/or vomiting; subjective blurring of vision of recent onset or an antecedent episode of intermittent blurring of vision with haloes. Patients also had at least 3 of 4 signs of an acute attack (corneal epithelial edema, an unreactive middledilated pupil, iris bombe©, and conjunctival hyperemia).

Identified cases of AAC were ineligible for participation if they had previous intraocular surgery in either eye, if they had a secondary cause for angle closure including neovascularization of the anterior segment, phacomorphic glaucoma (as defined by a white intumescent lens in the eye in which the attack occurred with a deep anterior chamber and open angles in the contralateral eye), and uveitis. Cases were also excluded if pilocarpine therapy was administered to the contralateral eye before our evaluation, if laser iridotomy was performed in the contralateral eye before enrollment in the study, or if they presented with bilateral AAC.

To ensure complete case ascertainment, we instructed the resident medical officers about the aims of the study and asked them to notify the study coordinator and research ophthalmologist (G.G. and J.D.) of any new cases seen each day. Furthermore, the study coordinator went to the emergency department daily to review the log of cases seen. The duty medical officer was contacted each morning to ensure maximum likelihood of identifying eligible cases.

CONTROL SELECTION

Controls were enrolled from a population-based prevalence survey of eye disease conducted on Chinese residents of the Tanjong Pagar district, adjacent to the Singapore National Eye Centre.1 These individuals were selected for the original prevalence survey using a disproportionate, stratified, clustered random-sampling procedure as described previously19 and are believed to be representative of the Chinese population of Singapore. They had been examined from January 6, 1997, through September 4, 1998, and a sample of these individuals (with an attempt to frequency match on the expected age and sex distribution of patients with AAC) was invited to return to the clinic for further testing. Controls were ineligible if they had undergone prior intraocular surgery in either eye before the prevalence survey was conducted.

Controls were evaluated at the slitlamp as part of an eye disease prevalence survey conducted 10 to 54 months before evaluation by Scheimpflug photography and ultrasonographic biomicroscopy (UBM). For this study, these controls were invited back to the Singapore National Eye Centre for additional testing using Scheimpflug photography and UBM and did not undergo a second evaluation at the slitlamp. Cases, however, were examined at the slitlamp at the same time that Scheimpflug photography and UBM were performed. The techniques used for slitlamp examinations of the cases were identical to those used for evaluation of controls, and the ophthalmologists performing the examinations were standardized against each other. A total of 3 ophthalmologists (G.G., P.F., and J.D.) participated in examining subjects for this study.

EXAMINATION TECHNIQUES

All cases and controls underwent a detailed eye examination including measurement of visual acuity, slitlamp examination, gonioscopy, A-scan ultrasonographic biometry, digital imaging with the Scheimpflug camera (Nidek EAS-1000; Nidek Co Ltd, Gamagori, Japan), and UBM (model 840; Zeiss-Humphrey, Dublin, Calif).

Optical ACD

This was performed using the pachymeter (Haag-Streit USA Inc, Mason, Ohio) with the corneal thickness measured with instrument I in all subjects. The dedicated eyepiece for the photographic slitlamp was used on position I. In addition, for corneal thickness, device I using a ×1.6 objective was used with a +2.5-diopter (D) eyepiece addition, and for ACD (including
The limbal chamber depth was graded in each eye using the incident beam, using the was viewed through the microscope at an angle of 60° to the ocular surface was used. The anterior chamber angle was measured in each eye using the Foster et al\textsuperscript{18} modification of the van Herick classification, with reference to standard photographs. Possible grades were 0%, 5%, 15%, 25%, 40%, 75%, and 100% of corneal thickness.

Limbal ACD (Modified van Herick)

The temporal limbus only was measured. The brightest, narrowest slit beam directed at the temporal limbus perpendicular to the ocular surface was used. The anterior chamber angle was viewed through the microscope at an angle of 60° to the incident beam, using the ×25 objective, from the nasal aspect. The limbal chamber depth was graded in each eye using the Foster et al\textsuperscript{18} modification of the van Herick classification, with reference to standard photographs. Possible grades were 0%, 5%, 15%, 25%, 40%, 75%, and 100% of corneal thickness.

Gonioscopy

Gonioscopy was performed after all other slitlamp testing so as not to adversely influence any measures. The Goldmann 2-mirror lens was applied to the anesthetized cornea using 0.5% hydroxy propyl methyl cellulose as a coupling agent. A dim beam was used where possible with illumination increased when unable to see structures because of low light. The illumination column was offset horizontally with a vertical beam for examination of the superior and inferior angles, and this column was vertically tilted with a horizontal beam for examination of the medial and lateral angles. The appearance of the drainage angles in each quadrant was recorded using the Spaeth classification.\textsuperscript{20} In addition, the angle was classified as open or narrow using a modified Scheie classification (according to the structures visible\textsuperscript{20}), which has been used in several major epidemiological studies of angle-closure glaucoma.\textsuperscript{21} If a closed angle was detected (ie, no visible pigmented trabecular meshwork in a quadrant), indentational (using a Sussman 4-mirror lens) or manipulative gonioscopy (using a Goldmann 1-mirror lens) was performed to assess the presence and extent of peripheral anterior synchiae and pigment in the superior trabecular meshwork. These were graded present or absent in each quadrant.

Corneal Curvature

For all controls and cases, corneal curvature was assessed using a handheld autorefractor keratometer (Retinomax K-plus; Nikon, Tokyo, Japan). The device recorded up to 8 separate estimates of corneal curvature along 2 meridians, each 90° apart. A mean value along each meridian was recorded. The mean corneal curvature was calculated as the average of the greater and lesser curvature.

A-Scan Biometry

Axial length, ACD, and lens thickness were measured using a 10-MHz A-mode ultrasonographic device (Storz Compuscan; Storz, Schweiz, Switzerland), which used a hard-tipped, corneal contact probe mounted on a Haag-Streit tonometer set to the intracocular pressure. The mean of 16 separate readings was recorded together with the SD of each parameter. An SD for axial length measurement of less than 0.13 mm was required. If the SD was greater, the reading was repeated up to another 2 times. When it was impossible to achieve an SD within these limits, these data were accepted but categorized as less reliable during analysis.

Digital Imaging

Images were obtained with the research nurse holding the eyelids apart using cotton-tipped applicators and making certain not to distort the globe. Two images were taken of all 4 quadrants on undilated eyes. Image analyses using the software provided with the machine to determine the anterior chamber angle width in degrees were performed by a single observer trained in measuring the anterior chamber angle. Reanalysis of 28 images obtained a mean (SD) difference of 1.1° (0.4°) for the average of all 4 angles.

Ultrasonographic Biomicroscopy

Images of the anterior chamber angles were obtained using the UBM (model 840; Zeiss-Humphrey) with a 50-MHz transducer probe. Patients were imaged in the supine position. Difficulty imaging the superior quadrant reproducibly led us to remove this measurement from the protocol. Hence, only images in the temporal, nasal, and inferior quadrants were obtained at each visit. After administering 0.4% benoxinate hydrochloride topical anesthesia, a plastic eyecup was used to gently part the eyelids and retain a layer of 2% methylcellulose coupling agent, with care not to exert pressure on the globe. Three standard axial image sections were obtained at the 3-, 6-, and 9-o’clock positions under standard lighting conditions (26.14 candela/m²). Variation in accommodation was minimized by fixation with the contralateral eye on a standard distance target on the ceiling.

The output of the UBM was stored on computer for analysis using the UBM Pro2000 software.\textsuperscript{21} A single observer performed all analyses 2 times. If the angle-opening distance (AOD) at 500 µm from the scleral spur differed by more than 10%, then a third analysis was performed on that image and the median value was used. To analyze the image using the UBM Pro2000 software, the operator identified the scleral spur. The software then automatically calculated the distance along a perpendicular line drawn from the corneal endothelial surface to the iris at 250, 500, and 750 µm (yielding the AOD of 250, 500, and 750 µm, respectively). The total area bounded by the iris and cornea at 750 µm from the scleral spur was calculated as the angle-recess area (Figure 1).

In addition, the observer subjectively graded the iris configuration as concave, flat, mildly convex, and extremely convex. The median of the 3 angles was chosen as the final iris configuration grade.
Figure 2. Entry of individuals with acute angle closure into the Singapore Case-Control Study of Acute Angle Closure.

Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases</th>
<th>Control Subjects</th>
<th>Controls for UBM and Scheimpflug Photography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD), y</td>
<td>63.7</td>
<td>58.6 (11.1)</td>
<td>64.9 (8.5)</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>69.9</td>
<td>50.7</td>
<td>50.4</td>
</tr>
<tr>
<td>Education†</td>
<td>20.4</td>
<td>35.7</td>
<td>28.8</td>
</tr>
<tr>
<td>Housing‡</td>
<td>44.6</td>
<td>71.4</td>
<td>72.6</td>
</tr>
</tbody>
</table>

Abbreviation: UBM, ultrasonographic biomicroscopy.
*All variables are statistically significant when comparing control subjects with cases at *P* < .05.
†Percentage of subjects with a secondary school education or higher.
‡Percentage of subjects in 1-, 2-, or 3-bedroom public housing.

Dynamic Tests

Ultrasonographic biomicroscopy and Scheimpflug photography were performed 1 minute after the room lights were turned off. Specifically, the patient was imaged with the Scheimpflug camera first; both with the lights on and then 1 minute after the lights were turned off. Then the UBM was used to image the patient with the lights on and 1 minute after the lights were turned off. Finally, the patient was reimaged using the Scheimpflug camera and then the UBM 30 minutes after instilling a dose of 4% pilocarpine hydrochloride.

STATISTICAL ANALYSIS

Baseline univariate comparisons between participants and nonparticipants were performed using a *t* test for both controls and cases. *χ²* Analysis was used for categorical data. For data on ocular biometry obtained at the slitlamp and with the A-scan ultrasonograph, the entire population of controls who had not had previous intraocular surgery from the Tanjong Pagar Survey was analyzed. For parameters derived from the Scheimpflug camera and the UBM, only controls who returned to the clinic for these special tests were included in the analysis. Multiple logistic regression analysis was used to identify factors that remained predictive of nonparticipation. Linear regression analyses adjusting for possible confounders were performed as well. When presenting mean differences (adjusted for age and sex) in ocular biometry, we present the mean for each parameter using men who are of the mean age of the entire study group (60.6 years). Finally, although 6 individuals of non-Chinese ethnicity presented with AAC, the analysis was limited to Chinese cases because all controls were of Chinese ancestry. Including individuals of other races in the analyses did not alter the results significantly.

RESULTS

CASES

A total of 212 cases presented to the Singapore National Eye Centre with a potential diagnosis of AAC (Figure 2). Ninety-nine were eligible and participated in our study; 59 were ineligible, 24 had secondary angle-closure glaucoma (18 phacomorphic, 5 rubeotic, and 1 uveitic), 17 were bilateral, 4 had undergone prior surgery, 7 had had previous AAC attacks, 1 was seen after being diagnosed as having chronic PACG, and 1 was receiving long-term pilocarpine therapy prior to the AAC attack). Seven additional subjects were ineligible for a variety of factors including previous pneumatic retinopexy, a history of vitritis, and long-term pilocarpine therapy prior to the AAC attack. An additional 22 subjects were eligible but were excluded from the study. Fourteen received pilocarpine therapy in the contralateral eye prior to evaluation, 7 underwent laser iridotomy prior to evaluation, and 1 was dilated in the contralateral eye prior to our evaluation. Finally, 33 eligible subjects (21.6% of eligible subjects) declined enrollment in the study. Cases in the youngest and oldest age ranges tended to participate more often than those who refused. They were similar for sex.

CONTROLS

We had 2 control groups. (1) Prevalence controls: These were all persons examined in the original eye disease prevalence survey conducted in the Tanjong Pagar Survey. All analyses of ocular biometry (except for the UBM and Scheimpflug camera parameters) were conducted using prevalence controls. (2) Case-control controls: These individuals were a subset of the original Tanjong Pagar Survey population who were recalled for a second evaluation using the UBM and Scheimpflug camera. Prevalence controls were younger and more often male than were cases (Table 1). They also tended to be less well educated and to live in lower-quality housing than cases. These associations remained in a multivariate analysis adjusting for age and sex. Case-control controls were older than the nonelected controls, had more years of education, had lower-quality housing, and were more often female. After adjusting
for age and sex, case-control controls had axial length, lens thickness, keratometry, and van Herick grades \((P > .05)\) similar to the prevalence controls. The age- and sex-adjusted optical ACD, however, was on average 0.06 mm deeper in case-control controls \((P < .05)\), and intraocular pressure was 1.0 mm Hg lower on average in case-control controls \((P < .05)\).

**OCULAR BIOMETRY**

Following successful treatment of the eye with symptomatic angle closure, we compared the contralateral eyes of cases with prevalence controls. Cases had shorter axial lengths, shallower ACD, thicker lenses, and steeper radii of corneal curvature \((P < .01, \text{Table 2})\). Furthermore, using multiple logistic regression to adjust for age and sex, patients with AAC were 19 times as likely to have a limbal ACD of 25% or less (95% confidence interval, 8.3–45.2 times as likely).

Lowe\(^{16}\) has proposed that the anterior lens position \([\text{ACD} + \frac{1}{2} \text{ lens thickness}] / \text{axial length}\) may explain the predisposition of some individuals to AAC. Cases had a relative lens position that was 0.008 more anterior than controls \((P < .05)\) which represents only a 4% difference from the average adjusted lens position of 0.21 for the controls. Kondo et al\(^{24}\) proposed that a small anterior chamber volume might be indicative of an eye at risk for AAC. Using the formula \(\pi (r d^2 - d^3) / 3\), where \(r\) is the radius of corneal curvature and \(d\) is the ACD, cases had lower volumes (94.7 mm\(^3\) vs 152.4 mm\(^3\), \(P < .001\)) after adjusting for age and sex.

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**Figure 3.** Boxplots of the distributions of anterior segment biometric parameters in acute angle closure attack and control eyes from the Singapore Case-Control Study of Acute Angle Closure. Circles are observations outside of 1.5 \(\times\) IQR (interquartile range, any points beyond the horizontal lines). The box shows the 25th and 75th percentiles; horizontal line, median value.
The AOD 500 µm on average 54% lower among cases, with a mean of 0.26 µm in controls, making for age and sex, the mean AOD 500 was 0.14 µm less was 0.18 µm for controls and 0.05 µm for cases. Adjust-

1 quadrant closed.

is only 50 µm). Cases were 29 times (95% confidence in-

vast majority of cases appeared closed by UBM in at least

UBM in at least 1 quadrant (although the resolution of the instrument is only 50 µm). Cases were 29 times (95% confidence in-
terval, 15.3-55.3) more likely than controls to have at least

1 quadrant (although the resolution of the instrument

UBM Response to Darkness

Both cases and controls demonstrated significant de-

clines in the AOD after the room lights were turned off for 1 minute (P <.05, Figure 6 and Table 3). After ad-

justing for age, sex, and AOD 500 µm with the lights on, the AOD 500 µm decreased more than twice as much in cases than in controls (P <.01, average decline in controls 0.012 µm, average decline in cases 0.029 µm, Table 3). Similar results were seen for the AOD 750 µm and for the angle-recess area.

Scheimpflug Camera Response to Darkness

The decline in the average angle width in the dark was less in cases than in controls (0.03° vs 0.51°). After ad-

justing for age, sex, and angle width with the lights on, the change was greater in cases, but of borderline statisti-
cal significance (P = .13, a 0.61° greater decrease in cases).

UBM Response to Pilocarpine Therapy

Both cases and controls demonstrated significant in-

creases in AOD 500 and 750 µm 30 minutes after a single

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A dose of 4% pilocarpine hydrochloride was administered (Figure 7 and Table 3). Cases had almost 50% less increase in the AOD (500 µm) when pilocarpine was given after adjusting for age and sex ($P<.05$, mean adjusted increase 0.039 in controls, 0.022 in cases, Table 3). Similar results were seen for AOD 750 µm and for angle-recess area.

Scheimpflug Camera Response to Pilocarpine Therapy

After adjusting for age, sex, and angle width prior to 4% pilocarpine therapy, the angle width increased by 1.2° on average in controls and decreased by 1.8° in cases ($P<.01$).

Figure 5. Boxplots of the distribution of angle width as measured using a Scheimpflug camera (Nidek EAS-1000; Nidek Co Ltd, Gamagori, Japan) in acute angle closure and control eyes from the Singapore Case-Control Study of Acute Angle Closure. Circles are observations outside of $1.5 \times$ IQR (interquartile range, any points beyond the horizontal lines). The box shows the 25th and 75th percentiles; horizontal line, median value.

Figure 6. Response to changing from light to dark conditions in the contralateral eye of an individual who had an acute angle-closure attack. A, Angle appearance in the light. B, Angle appearance in the dark.

To our knowledge, this is the largest reported series of patients with AAC studied prospectively in a systematic fashion. Since more than 50% of contralateral eyes are expected to develop AAC, their behavior may offer a unique insight into the mechanism of AAC. We compared contralateral AAC eyes with matched population controls to study differences that would be most valid. Our findings not only supported previous conclusions about anatomical features of AAC-affected eyes, they point to important physiological differences that extend our understanding of this condition.

We found that the contralateral eyes of patients with AAC are anatomically different from controls in ways that predispose to impaired aqueous humor circulation. These include features of the axial length, cornea, anterior chamber, and lens. Axial length was, on average, shorter in the contralateral eyes of patients with AAC than in controls, which is consistent with previous work in several populations. The radius of corneal curvature was less in cases than in controls. Two previous reports in European-derived people with PACG had similar conclusions to our study, while 2 smaller studies (<20 cases of PAC) reported no difference. It is logical that steep corneal curvature combined with shallow ACD might lead to closer positioning of the iris root to the trabecular meshwork, making appositional closure more likely.

The lenses of cases were thicker than those of controls even after adjusting for age. This is consistent with previous reports on patients with angle closure from European, Chinese, Bantu, and Indian populations. The lenses were, on average, 0.34 to 0.65 mm thicker in cases than controls in those reports. A thicker lens would be expected to exacerbate resistance to aqueous movement through the channel between the iris and lens at the pupil. An analysis by Tiedeman showed that the more anterior the position of the lens, the more the iris bows anteriorly.

The combination of smaller axial lengths, steeper corneal curvatures, and thicker lenses is reflected in the
shallower ACD of AAC cases, with only 15% of cases having an ACD exceeding 2.1 mm. These findings are consistent with previous reports of the ACD in patients with angle closure.5,10,11,26,31 Lowe10,16 proposed combining ACD data with lens thickness and axial length to arrive at a summary measure, called the relative position of the lens \[ \frac{(ACD + \frac{1}{2} \text{ lens thickness})}{\text{axial length}} \]. While this parameter was associated with AAC in our study, the relative position of the lens was only slightly more anterior in AAC cases than in controls. Calculated anterior chamber volume, however, was considerably smaller in cases than in controls, a result that may derive from the fact that volumetric measures increase by a power of the ACD.

The angle appearance as measured using limbal ACD, UBM, and Scheimpflug photography was significantly narrower in AAC cases. The van Herick assessment of chamber depth using an angled, slitlamp beam at the limbus demonstrated large differences between cases and controls, as previously reported.12,20,32 Among the UBM parameters, the AOD at 500 and 750 µm were better at separating cases from controls than the AOD at 250 µm or the integral of angle area (angle-recess area). The Scheimpflug angle width also showed large differences between cases and controls, once again indicating that the angle is significantly narrower in the contralateral eyes of cases. Yet, there were still areas of overlap between cases and controls for each of the anatomical parameters.

The Chinese population has more than 5 times the rate of PACG compared with European-derived populations. Since smaller eyes with smaller anterior chambers are predisposed to PACG, it might be considered likely that Chinese people would be more likely to have this susceptible anatomy. In direct contradiction to this prediction, Congdon et al13 found that the ocular anatomical parameters (ACD, axial length, and refractive error) have indistinguishable distributions in European-derived, African-derived, and Taiwanese Chinese persons. However, others have found shallower ACDs among peoples with higher rates of PACG.12 If Chinese individuals do not have shallower ACDs on a population basis, then other factors are responsible for the higher prevalence and incidence rates seen. In population-based data, it has been estimated that among 10 people with narrow chamber angles, approximately 1 will ultimately develop PACG. Our data point to the need to investigate the dynamic behavior of eyes at risk for angle closure, not just their anatomy. Despite highly detailed and technologically advanced examinations, as performed here, anatomical measurements cannot predict physiological dysfunction.

In fact, contralateral eyes of AAC cases showed dynamic differences from age-matched, control eyes, even when comparing eyes in both groups that begin with the same narrow angle. With UBM imaging, cases had greater shallowing when placed in the dark for 1 minute. This was consistent in all 3 quadrants of the angles studied, and using all UBM parameters. Furthermore, while not statistically significant, a modest trend for the same finding was seen with Scheimpflug imaging. Likewise, 4% pilocarpine eyedrops caused less deepening of the angle in AAC cases than in controls. Each of these behaviors shows fundamentally different responsiveness of AAC affected eyes in a manner that would be more likely to cause angle occlusion. Responses such as these may prove to identify AAC- and PACG-affected eyes as provocative tests. They suggest that the iris and lens in affected eyes act in a manner that makes angle occlusion more likely. Past provocative testing attempted to measure dysfunction using increase in intraocular pressure as the outcome measure. More direct measures of physiological difference may be better predictors.

Other physiological responses of the iris and lens in PACG not investigated in the current study may play a role in the development of PACG. It is clinically apparent that forward movement of the iris-lens diaphragm is characteristic of PACG-affected eyes, both intraoperatively (so-called positive pressure) and in a greater tendency to flat chamber after glaucoma filtering surgery. One recently proposed hypothesis is that expansion of the choroid could transmit a pressure differential to the anterior structures (H.A.Q., unpublished data, 2002). Choroidal expansion is a cause of angle closure when inflammation, tumors, bleed-
ing, or high orbital venous pressure are grossly present. Choroideal expansion has been detected in eyes with AAC and in malignant glaucoma. An expansion of only 20% in choroidal volume (about 50-µm increase in thickness) would occupy more than 100 µL of space in the eye—a volume equal to the entire anterior chamber volume in an eye with the typical anatomy for PACG. These considerations, as well as other potential risk factors, such as ciliary body position and flexibility, and laxity of the lens zonule, deserve active investigation as physiological participants in the PACG mechanism.

This study has several limitations. The sample of controls studied by UBM and Scheimpflug photography was a subset of the prevalence study controls. While most ocular parameters were similar between the 2 groups, the optical ACD was slightly greater in the sampled controls. While this 0.06-mm difference is not clinically significant, it indicates that some with shallow ADCs may have been excluded from the sampled group. This is likely since all individuals with occludable angles identified in the prevalence survey were referred for further clinical assessment and possible laser iridotomy and, therefore, ineligible to be sampled for imaging. This group was small, but nevertheless, it is possible that the differences observed between cases and controls using the machine-derived parameters may be overestimates. However, all other parameter estimates were based on the entire population-based sample and were not influenced by this treatment decision. A second limitation is that we could not enroll all cases. Some refused, and others received therapy before enrollment. Although the usual reason for premature treatment was simply that the managing ophthalmologist forgot to notify the study coordinator, it is possible that medical staff selected some of the more severe cases for early contralateral prophylaxis and this may have removed those cases from the pool. This would likely have tended to decrease the differences seen between cases and controls. A third limitation is that the cases and controls were examined at the slitlamp by different observers in most instances. Extensive training to standardize these observers was undertaken, with high κ values previously reported between 2 of the 3 ophthalmologists. Similar κ values were found for the third ophthalmologist (G.G.) when compared with the others.

There are several strengths to the present study. All subjects were enrolled prospectively, and all incident cases were approached. More than 50% of all incident cases in Singapore report to the Singapore National Eye Centre where the research was conducted, and the age, race, and sex distribution of these cases is similar to those that present at other institutions throughout the island. There is little reason to suspect selection bias in the cases who presented. The use of population-based controls avoids the many biases that may be seen with clinic-based controls. Finally, we used standardized examination techniques throughout the study when obtaining biometric data on study participants.

CONCLUSIONS

We have found that contralateral eyes of individuals suffering AAC are measurably shorter, have thicker lenses, have steeper radii of corneal curvature, have shallower central anterior chambers, and have more crowded filtering angles. Furthermore, when placed in the dark, contralateral eyes experienced greater shallowing, and when given 4% pilocarpine therapy, contralateral eyes deepen less than normal control eyes. These findings suggest the need to investigate new mechanisms in AAC and may lead to more effective screening strategies in the future.

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REFERENCES


Congratulations to the winner of our February quiz, Leonardo Torqueti Costa, MD, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil. The correct answer to our February challenge was congenital anomalous retinal artery and leaking macroaneurism. For a complete discussion of this case, see the Clinicopathologic Reports, Case Reports, and Small Case Series section in the March ARCHIVES (Chalam KV, Gupta SK, Vinjamur S, Shah VA. Congenital anomalous retinal artery associated with leaking macroaneurism. Arch Ophthalmol. 2003;121:409-410).

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