**Association of Narrow Angles With Anterior Chamber Area and Volume Measured With Anterior-Segment Optical Coherence Tomography**

Ren-Yi Wu, MD, PhD; Monisha E. Nongpiur, MD; Ming-Guang He, MD, PhD; Lisandro M. Sakata, MD; David S. Friedman, MD, PhD; Yong-Huak Chan, PhD; Raghavan Lavanya, MD; Tien-Yin Wong, MD, PhD; Tin Aung, MBBS, PhD

**Objectives:** To describe the measurement of anterior chamber area and anterior chamber volume by anterior-segment optical coherence tomography and to investigate the association of these parameters with the presence of narrow angles.

**Methods:** This was a cross-sectional study of subjects aged at least 50 years without ophthalmic symptoms recruited from a community clinic. All participants underwent standardized ocular examination and anterior-segment optical coherence tomography. Customized software was used to measure anterior chamber area (cross-sectional area bounded by the corneal endothelium, anterior surface of iris, and lens within the pupil) and anterior chamber volume (calculated by rotating the anterior chamber area 360° around a vertical axis through the midpoint of the anterior chamber area). An eye was considered to have narrow angles if the posterior pigmented trabecular meshwork was not visible for at least 180° on gonioscopy with the eye in the primary position.

**Results:** A total of 1922 subjects were included in the final analyses, 317 (16.5%) of whom had narrow angles. Mean anterior chamber area (15.6 vs 21.1 mm²; P < .001) and anterior chamber volume (97.6 vs 142.1 mm³; P < .001) were smaller in eyes with narrow angles compared with those in eyes without narrow angles. After adjusting for age, sex, anterior chamber depth, axial length, and pupil size, smaller anterior chamber area (odds ratio, 53.2; 95% confidence interval, 27.1-104.5) and anterior chamber volume (odds ratio, 40.2; 95% confidence interval, 21.5-75.2) were significantly associated with the presence of narrow angles.

**Conclusion:** Smaller anterior chamber area and anterior chamber volume were independently associated with narrow angles in Singaporeans, even after controlling for other known ocular risk factors.

Arch Ophthalmol. 2011;129(5):569-574

**PRIMARY ANGLE-CLOSURE glaucoma (PACG) is a major cause of visual morbidity, especially in East Asia.**1-4 Detection of risk factors and early markers for PACG is necessary for formulating strategies for screening, prevention, and treatment of this disease. Several studies have previously reported ocular biometric risk factors for PACG, such as a shallow anterior chamber depth (ACD), thick and anteriorly placed lens, and short axial length (AL).5-8 We recently conducted a study in Singapore that demonstrated the strongest predictors for angle closure were female sex, shorter AL, shallower ACD, and Chinese race/ethnicity.6 However, sex and racial differences for risk of angle closure were not fully explained by variations in AL or ACD alone,6 suggesting that risk factors other than those observed may be important.

Anterior-segment optical coherence tomography (AS-OCT) permits imaging of the entire cross-section of the anterior segment in 1 image frame, allowing measurements of the entire anterior segment. We recently identified novel associations of AS-OCT–defined iris parameters (such as increased iris thickness and cross-sectional area) with the presence of narrow angles.9 Two other novel parameters, neither of which requires subjective input to be derived from AS-OCT images, are cross-sectional anterior chamber area (ACA) and anterior chamber volume (ACV). To our knowledge, they have not been studied in terms of their relationship with narrow angles and/or angle closure. We report here the distribution and determinants of ACA and ACV in a large sample of subjects recruited from a community clinic, as well as the relationship of ACA and ACV with narrow angles in this population.

**METHODS**

Approval for the study was granted by the Institutional Review Board of the Singapore Eye Re-
search Institute, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent for this research was obtained from all subjects before enrollment.

Subjects aged at least 50 years were recruited from a government-run polyclinic that provides primary health care services for residents living in the area around the clinic. Details of the study have been described previously.6,8,9 Briefly, subjects were identified by systematic sampling (every fifth patient registered at the polyclinic who met the study eligibility criteria). A detailed questionnaire was administered that included demographic and socioeconomic details, educational level, and medical and ocular history. Recruited subjects did not have any ophthalmic complaints, and individuals with a history of glaucoma, previous intraocular surgery, previous laser treatment, penetrating eye injury, or corneal disorders preventing anterior chamber assessment were excluded.

All subjects underwent a detailed eye examination that included visual acuity measurement using a logarithm of minimum angle of resolution chart (logMAR chart; Lighthouse Inc, Long Island, New York), slitlamp examination (model QQ 900; Haag-Streit, Bern, Switzerland), stereoscopic optic disc examination with a 78-diopter lens (Volk Optical Inc, Mentor, Ohio), and intraocular pressure measurement with Goldmann applanation tonometry (Haag-Streit, Koniz, Switzerland). Axial length and central ACD were measured by IOLMaster (Carl Zeiss, Jena, Germany). Gonioscopy was performed in the dark by a single fellowship-trained glaucoma specialist (R.L.) using a Goldmann 2-mirror lens at high magnification (×16). Indentation gonioscopy with a Sussman 4-mirror lens (Ocular Instruments Inc, Bellevue, Washington) was used to establish the presence or absence of peripheral anterior synchiae. An eye was considered to have narrow angles if the posterior pigmented trabecular meshwork was not visible for at least 180° on nonindentation gonioscopy with the eye in the primary position.

AS-OCT IMAGING

All subjects underwent imaging with AS-OCT (Visante; Carl Zeiss Meditec, Dublin, California) under standardized dark conditions by an operator who was masked to the results of the clinical ophthalmic examination.5,8,9 Scans were centered on the pupil and taken along the horizontal axis (nasal-temporal angles at 0° to 180°) using the standard anterior segment single-scan protocol. To obtain the best quality image, the examiner adjusted the saturation and noise and optimized the polarization for each scan during the examination. Because several scans were acquired by the AS-OCT device, the examiner chose the best image, with neither motion artifacts nor image artifacts due to the eyelids.

One cross-sectional horizontal AS-OCT scan of the nasal and temporal angles was evaluated for each subject. These images were then processed using customized software, the Zhongshan Angle Assessment Program (Guangzhou, China),10 by study ophthalmologists (L.M.S. and R.-Y.W.) who were masked to clinical data. The algorithm then automatically calculated the ACA and ACV. With this program, the ACA (Figure) was defined as the cross-sectional area of anterior segment bounded by endothelium, anterior surface of iris, and anterior surface of lens (within the pupil). A vertical axis through the midpoint (center) of the ACA was plotted by the program, and the ACV was calculated by rotating the ACA 360° around this vertical axis (Figure).

Intragrader and intergrader reliability of ACA and ACV measurement were assessed in 30 randomly selected AS-OCT images (25 with and 25 without narrow angles). The intraclass correlation coefficient and the limit of agreement (LOA; mean of differences ± 1.96 × standard deviation of differences) were calculated.

STATISTICAL ANALYSIS

Right eyes were used for analysis. Statistical analysis was performed using the statistical package STATA, version 9.2 (StataCorp LP, College Station, Texas). The ACA and ACV were compared between sexes and between eyes with and without narrow angles. Because anterior segment biometric parameters are well known to be associated with age and sex, the association of ACA and ACV with the presence of narrow angles (gonioscopy) was evaluated using logistic regression models to determine the odds ratio and 95% confidence interval (CIs), after adjusting for age and sex. The multivariate adjusted odds ratio and 95% CI were obtained after adjustment for age, sex, AL, central ACD, and pupil size. Multivariate adjusted odds ratios were also calculated after stratifying by age and sex groups because the effect seemed to vary on the basis of these parameters. Cross-product terms for age and sex were also included in models for the whole cohort to formally test for interaction. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of ACA and ACV for identifying narrow angles were calculated. Receiver operating characteristic curves were generated, and the area under the curve (AUC) was used to assess the perfor-
RESULTS

A total of 2047 community-based subjects were recruited, of which 125 (6.1%) were excluded from analysis for the following reasons: 5 subjects (0.2%) could not undergo gonioscopy, 63 subjects (3.1%) could not complete AS-OCT examination or had poor-quality AS-OCT images, and 57 subjects (2.8%) had Zhongshan Angle Assessment Program software delineation errors. Of the 1922 subjects (93.9%) who were included for the final analysis, 1007 (52.4%) were female and 1717 (89.3%) were Chinese (Table 1). In brief, compared with those included, excluded subjects were significantly older and had shallower ACD, and there were proportionately more subjects with gonioscopic narrow angles.

The mean ACA was 20.1 mm² (range, 10.4-33.6 mm²), and the mean ACV was 134.8 mm³ (range, 56.6-242.1 mm³) (Table 2). Mean ACA (19.6 vs 20.8 mm²; P < .001) and ACV (129.7 vs 140.4 mm³; P < .001) were significantly smaller in women than in men. Both ACA (P for trend < .001) and ACV (P for trend < .001) were found to decrease significantly with age.

A total of 317 subjects (16.5%) were diagnosed as having narrow angles on gonioscopy. Eyes with narrow angles had a significantly smaller ACA (15.6 vs 21.1 mm²; P < .001) and ACV (97.6 vs 142.1 mm³; P < .001) compared with those without narrow angles. Approximately 60% of subjects within the first quartile of ACA or ACV had narrow angles (Table 3). Previous data obtained from the same study population indicated that there were significant differences between narrow-angle and open-angle subjects in terms of age, sex, AL, and ACD, and therefore these variables were included in the multivariate models to assess for independent association between ACA and ACV measurements and narrow angles (Table 4). After adjustment for age, sex, AL, central ACD, and pupil size, the adjusted odds ratios (95% CI) for per-SD increase of ACA and ACV were 53.2 (27.1-104.5) and 40.2 (21.5-75.2), respectively. Women generally had stronger associations for ACA and ACV compared with those of men. Similarly, associations were stronger in subjects younger than 60 years. However, all
age and sex interactions were not significant (data not shown).

Subgroup analysis based on ethnicity in this study population revealed that the mean ACA for Chinese, Malay, Indian, and other races was 20.1, 20.2, 20.8, and 20.6 mm², respectively, whereas the mean ACV was 134.3, 134.4, 139.9, and 138.1 mm³, respectively. Significant difference in ACA and ACV was observed only between the Chinese and Malay subjects, even after adjustment for age and sex (data not shown).

For the detection of eyes with narrow angles, the optimal cutoff was determined for measurements of ACD (cutoff ≤2.95 mm; AUC, 0.828; 95% CI, 0.805-0.852), ACA (cutoff ≤17.9 mm²; AUC, 0.877; 95% CI, 0.856-0.899), and ACV (cutoff ≤116.0 mm³; AUC, 0.877; 95% CI, 0.855-0.898). Anterior chamber area and ACV had identical AUCs, which was significantly better (P < .001) than ACD in detecting narrow angles. Tests of performance of each measurement, as well as their combinations, are shown in Table 3. When the cutoff for specificity was set at 90%, the sensitivity was 85.5% for ACA, 85.2% for ACV, and 73.5% for ACD.

All intragrader and intergrader intraclass correlation coefficients for ACA and ACV were 1.0. The intragrader LOA for ACA was from −0.046 to 0.054, with a mean difference of 0.007, and the intergrader LOA for ACA was from −0.082 to 0.092, with a mean difference of 0.034. The intragrader LOA for ACV was from −0.089 to 0.111, with a mean difference of 0.034, and the intergrader LOA for ACV was from −1.325 to 1.186, with a mean difference −0.070. The upper and lower values of LOAs were less than 1% for ACA and less than 1.5% for ACV of the corresponding overall means. These results suggest excellent reproducibility of ACA and ACV measurement by Zhongshan Angle Assessment Program software on AS-OCT images.

### Table 3. Prevalence of Narrow Angles by ACA and ACV Quartiles

<table>
<thead>
<tr>
<th>Measure, Quartile</th>
<th>No. of Subjects</th>
<th>Narrow Angles, No. (%) of Subjects Within the Quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA, mm²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (&lt;17.72)</td>
<td>484</td>
<td>272 (56.2)</td>
</tr>
<tr>
<td>2 (17.73-20.01)</td>
<td>478</td>
<td>44 (9.2)</td>
</tr>
<tr>
<td>3 (20.02-22.49)</td>
<td>480</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>4 (&gt;22.49)</td>
<td>480</td>
<td>0</td>
</tr>
<tr>
<td>ACV, mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (&lt;114.0)</td>
<td>480</td>
<td>278 (57.9)</td>
</tr>
<tr>
<td>2 (114.1-132.4)</td>
<td>481</td>
<td>39 (8.1)</td>
</tr>
<tr>
<td>3 (132.5-154.3)</td>
<td>481</td>
<td>0</td>
</tr>
<tr>
<td>4 (&gt;154.3)</td>
<td>480</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: ACA, anterior chamber area; ACV, anterior chamber volume.

### Table 4. Relationship of ACA and ACV and Narrow Angles, by Sex and Age Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>All</th>
<th>Men</th>
<th>Women</th>
<th>&lt;60 y</th>
<th>≥60 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA, per SD increase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR1 (95% CI)³</td>
<td>32.3 (22.1-47.4)</td>
<td>28.9 (16.3-51.4)</td>
<td>35.3 (21.2-58.9)</td>
<td>42.0 (20.6-85.5)</td>
<td>32.3 (22.1-47.4)</td>
</tr>
<tr>
<td>OR2 (95% CI)³</td>
<td>53.2 (27.1-104.5)</td>
<td>39.3 (14.0-109.9)</td>
<td>64.4 (26.3-158.0)</td>
<td>87.3 (27.2-260.3)</td>
<td>45.6 (19.3-107.7)</td>
</tr>
<tr>
<td>ACV, per SD increase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR1 (95% CI)³</td>
<td>37.3 (25.1-55.7)</td>
<td>33.2 (18.2-60.7)</td>
<td>40.7 (23.9-69.2)</td>
<td>50.8 (23.9-108.0)</td>
<td>35.8 (25.1-55.7)</td>
</tr>
<tr>
<td>OR2 (95% CI)³</td>
<td>40.2 (21.5-75.2)</td>
<td>26.2 (10.3-67.0)</td>
<td>54.5 (23.6-126.2)</td>
<td>69.8 (22.1-219.9)</td>
<td>33.7 (15.5-73.1)</td>
</tr>
</tbody>
</table>

Abbreviations: ACA, anterior chamber area; ACV, anterior chamber volume; CI, confidence interval; OR, odds ratio.

³Adjusted for age and/or sex.

To effectively prevent PACG by the use of prophylactic laser iridotomy, it is necessary to identify people with early stages of the disease. Early detection of anatomically narrow angles is therefore an important component of future blindness-prevention programs in Asia. It has been well documented that some ocular parameters, such as ACD and AL, reveal risk factors for PACG. A recent study also showed that ACV, when measured by Penticam (Oculus, Wetzlar, Germany), was significantly correlated with angle width (Shaffer grade) by gonioscopy in a group of 72 Japanese angle-closure suspects. However, studies with large populations have not been performed to evaluate the potential of ACV in detecting narrow angles. In this study, smaller ACA and ACV were independently associated with narrow angles, even after accounting for ACD, AL, and other known associated systemic and ocular biometric parameters. These data suggest novel associations between ACA/ACV and narrow angles.

Interestingly, after stratifying by age and sex and adjusting for other known risk factors, ACA and ACV showed a stronger association with narrow angles in women than in men and in those younger than 60 years than in those of an older age. Although the precise biologic/physiologic explanations for these differences remain to be determined, these observations may partly explain the observation that narrow angles are more often seen in women. Because ACA/ACV is the area/volume bounded by the cornea, the iris, and the anterior surface of the lens, the change in ACA/ACV is the composite result of changes in these tissues. Increasing lens thickness with age may be an important factor causing the age-related decline in these parameters. The relationship of ACA/ACV with other ocular biometric parameters needs further investigation. In the present study, we also found that ACA and ACV were smallest in Chinese adults compared with those of other races. We speculate that smaller ACA and ACV in Chinese persons may in part explain the observation that Chi-
nese persons have a higher risk of angle closure. Furthermore, studies on interethnic differences in ACA/ACV and risk of angle closure may shed light on the pathophysiologic characteristics of PACG.

Several ocular biometric measurements, such as ACD, have been evaluated as screening parameters for angle closure. Theoretically, the ideal community-based screening test should be physician independent, quick, and noninvasive and should have a very high specificity. When we attempted to assess the performance of AS-OCT–measured ACA/ACV in detecting narrow angles, we found that ACA (cutoff of 17.9 mm²) and ACV (cutoff of 116.0 mm³) had equal AUC (0.877). Comparing OCT–measured ACA/ACV in detecting narrow angles, it may be differences in ACV estimates if superior-inferior scans were used.

In summary, in this large community-based study, we found that smaller ACA and ACV were independently associated with the presence of narrow angles, even after controlling for other known ocular risk factors, such as ACD. Associations were generally stronger in women and in people younger than 60 years. Our findings highlight the need for further research into the specific role of ACA and ACV in angle-closure pathogenesis and whether these parameters are useful for screening.

Submitted for Publication: April 5, 2010; final revision received July 1, 2010; accepted August 1, 2010.

Correspondence: Tin Aung, MBBS, PhD, Singapore National Eye Centre, 11 Third Hospital Ave, Singapore 168751 (tin11@pacific.net.sg).

Financial Disclosure: Dr Aung has received research funding, travel support, and honoraria from Carl Zeiss Meditec. Dr Friedman has received an instrument loan from Carl Zeiss Meditec.

Funding/Support: This study was supported by grant NRMC/CSA/004/2008 from the National Medical Research Council, Singapore, and grant NRMC/TCR/002/SERI/2008 from the National Research Foundation, Singapore.

REFERENCES


2. Foster PJ, Baasanhu J, Alsbirk PH, Munkhbayar D, Uranchimeg D, Johnson GJ.


Ophthalmological Numismatics

A student of Cornelius Donders in Utrecht, Herman Snellen (1834-1908) received his medical degree in 1857 and thereafter worked at the Netherlands Ophthalmic Hospital until he was made professor at the University of Utrecht in 1877. From 1884 to 1903 he succeeded Donders as the director of the Netherlands Ophthalmic Hospital. Although Snellen improved and invented a number of surgical procedures, including those for entropion, ectropion, and trichiasis, today he is best known for the vision letter-chart tests that bear his name. His son, Herman Snellen Jr, also became a professor of ophthalmology at Utrecht.

In 1938, to commemorate the centennial of the Royal Netherlands Ophthalmic Hospital and the 50th anniversary of Snellen’s death, this medal was commissioned as an award to be presented to a Dutch ophthalmologist annually for important work in ophthalmology. The medal was designed by the artist J. C. Hekman and was struck in bronze in 103-mm diameter. The obverse depicts Snellen’s clothed bust left. Specimens were also produced in ceramic.

Courtesy of: Jay M. Galst, MD, Clinical Associate Professor, New York Medical College, and Peter van Alfen, PhD, Associate Curator, American Numismatic Society.

Correspondence: Jay M. Galst, MD, 30 E 60th St, New York, NY 10022.