Anterior Chamber Depth Measurement as a Screening Tool for Primary Angle-closure Glaucoma in an East Asian Population

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Objective: To evaluate anterior chamber depth measurement as a method of screening for primary angle-closure glaucoma in an East Asian population.

Design: Two-phase, cross-sectional, community-based study.

Setting: Rural and urban locations in the Hövsgöl and Ömnögobi provinces, Mongolia.

Participants: Nine hundred forty-two (94.2%) of 1000 individuals in Hövsgöl (1995) and 775 (96.9%) of 1000 individuals in Ömnögobi (1997) aged 40 years or older were examined.

Main Outcome Measures: Anterior chamber depth was measured by optical pachymetry, slitlamp-mounted A-mode ultrasound, and handheld ultrasound. Gonioscopy was used to detect occludable angles, defined as one in which the trabecular meshwork was visible for less than 90° of angle circumference. Primary open-angle glaucoma was diagnosed in subjects with an occludable angle and glaucomatous optic neuropathy with visual morbidity. The area under the curve in a receiver operating characteristic plot was used to compare test performance.

Results: Optical pachymetry outperformed the slitlamp-mounted ultrasound method of anterior chamber depth measurement (area under the curve, 0.93 and 0.90, respectively; z test, P = .001). Handheld ultrasound (area under the curve, 0.86) was inferior to optical measurement (z test, P = .001) but did not differ significantly from slitlamp ultrasound (z test, P = .06). The optical method gave sensitivity of 85% and specificity of 84% at a screening cutoff of less than 2.22 mm for detecting occludable angles.

Conclusions: Measurement of axial anterior chamber depth can detect occludable angles in this Asian population and therefore may have a role in population screening for primary angle-closure glaucoma.


THE ASSOCIATION between a shallow anterior chamber and primary angle-closure glaucoma (PACG) is well documented.1-4 The measurement of axial anterior chamber depth (ACD) may have potential in screening for PACG.3,5,6 The need for public health initiatives to combat PACG was highlighted by an estimate that half of the 67 million people suffering from primary glaucoma globally have PACG. It has been calculated that 6.7 million people worldwide have been irreversibly blinded as a consequence of glaucoma. Half of these are Asian, the majority ethnic Chinese.7 A means of detecting those at risk (people with occludable drainage angles) is a prerequisite of a prevention program. If an effective test can be identified, PACG may meet the criteria for viable population screening.8 Nd:YAG laser peripheral iridotomy probably represents a safe and effective prophylactic treatment.9

The most widely used method of ACD measurement in population-based research has been optical pachymetry. Although this technique is accurate and reproducible,1,10 it is not ideal for screening because it requires bulky equipment and is dependent on operator skill. We sought to compare optical pachymetry with 2 methods of ultrasound (US) measurement more practical for screening.

RESULTS

Of the 1800 subjects selected by the sampling frame, 1610 subjects (89.4%) were examined, 942 in Hövsgöl and 668 in Ömnögobi. However, because of practical difficulties (handwritten census data in Mongolian Cyrillic) in cross-checking selected subjects, a further 107 community-based
SUBJECTS AND METHODS

The Ministry of Health, Ulaanbaatar, Mongolia, gave ethical approval for this project. The work was performed in accordance with the World Medical Association’s Declaration of Helsinki.

SAMPLING

Between May 25 and August 25, 1995, 1000 subjects aged 40 years and older were selected for examination in the Mongolian province of Hovsgol. Clustered simple random sampling was used in urban centers, and systematic sampling was used in rural areas. The second phase of data collection was carried out in the Mongolian province of Omnogobi between July 28 and October 2, 1997. Dalanzadgad, the regional capital, was chosen as the urban study site. Sevrei was randomly selected from the 15 districts in Omnogobi as the rural study area. Local government census data were used to stratify the populations of these areas by age and sex. Approximately equal numbers of subjects were drawn from the age strata 40 to 49, 50 to 59, 60 to 69, and 70 years and older. The number of men and women selected was determined by their proportion in each decade age group. A total of 800 subjects were selected, 560 from Dalanzadgad and 240 from Sevrei (Table 1). This represents 9.6% of the population of Omnogobi aged 40 years and older and 33.7% of the combined populations of Dalanzadgad and Sevrei in this age group.

OPHTHALMIC ASSESSMENT

Central ACD (corneal epithelium to anterior lens epithelium) and central corneal thickness were measured at the slitlamp (model 900; Haag-Streit, Bern, Switzerland) by optical pachymetry (Depth Measuring Devices 1 and 2; Haag-Streit). “True” ACD (corneal endothelial surface to anterior lens surface) was calculated by subtracting the corneal thickness from the central ACD measurement and was used in further analysis. No correction was made for corneal radius or diameter. No cycloplegic agents were used before measurements were taken. The intraocular pressure (IOP) was measured 3 times in each eye by means of an applanation tonometer (Goldmann model; Haag-Streit). The median of the 3 readings was taken as the IOP for that eye. Slitlamp-mounted US was used in 1995, and all examinations were performed by 1 examiner (P.J.F.). In 1997, any one of the examining team in that year (J.G.D., D.M., D.U., T.E.) performed handheld US. The same model of US machine was used throughout (Allergan-Humphrey model 820 ultrasonic biometer; Allergan, London, England). Care was taken not to indent the cornea. Five readings were taken from each eye, and the single best trace from each eye was used.

Goldmann 2-mirror gonioscopy was performed on all subjects. The drainage angle was graded as either occludable or open (see “Diagnostic Classification” on next page). Manipulative and/or indentational gonioscopy with the Goldmann 2-mirror lens and Sussman 4-mirror lens, respectively, were used (except when the angle was wide open) to establish presence or absence of peripheral anterior synechiae. Excessive trabecular pigmentation in the superior angle was also noted.

The central visual field of all subjects was assessed by means of a semiautomated screening device (Henson CFA 3000; Tinsley Medical Instruments, Newbury, England). A 26-point static threshold-related suprathreshold test was performed. If 1 or more points were missed, this was extended to a 66-point test. Subjects with a field graded suspect or abnormal by the internal algorithm were retested by means of a 52-point threshold analysis. The vertical cup-disc ratio (CDR) was estimated and the posterior pole was examined through an undilated pupil with a +90-diopter subjects were recruited by the census office in Omnogobi. These additional subjects, giving a total of 1717 examined, are included in the results reported, as it was not possible to verify in all cases the subjects so selected. Excluding the 96 identifiable cases made no substantial difference to the results reported herein.

An occludable angle was detected in at least 1 eye of 140 subjects. Of these, 77 were classified as PACS, 35 as PAC, and 28 with PACG. Optical ACD measurement was possible in 1650 (96.1%) of the 1717 subjects. Among the 67 subjects for whom measurement was impossible, 1 had PACS, and 1 was normal. Subjects in whom ACD was not measured were omitted from the receiver operating characteristic analysis.

Table 2 summarizes the performance of the 3 tests in the detection of all occludable angles (PACS, PAC, and PACG). PAC and PACG combined, and PACG alone, giving sensitivity, specificity, and predictive values for the ACD where sensitivity and specificity are closest. Figures 2, 3, and 4 are receiver operating characteristic curves that compare the performance of the optical data (1995 and 1997 combined), slitlamp-mounted US, and handheld US in detection of all occludable angles, PAC and PACG combined, and PACG alone. Table 3 gives the AUC and the 95% confidence interval of the difference between the AUC of the curves compared, along with the z statistic and associated P values. In screening for each “disease entity” (occludable angles, PAC and PACG combined, and PACG alone), the trend was the same. The AUC was greatest for the optical method, then slitlamp-mounted US, and least with handheld US. The only exceptions were found in comparing optical 1997 data with slitlamp US data for detecting PACG and PAC combined or PACG alone. A significant difference was found only between optical pachymetry (1997) and hand-
COMMENT

Despite the acknowledged association between a shallow anterior chamber and closure of the drainage angle, there have been few studies exploring the role of ACD measurement in screening for PACG in a community setting. Table 4 summarizes results of studies in which sensitivity and specificity figures are cited or calculated from published data. Although comparison is difficult because of differing methods, the studies in Greenland, Taiwan, and Mongolia (reported herein) produced comparable sensitivity and specificity. The cutoff values chosen for Mongolians and Inuit differ slightly (<2.22 and <2.00, respectively). This difference in cutoff value might be expected as age-specific mean ACD is shallower in the Inuit people, who also have a higher prevalence of PACG. The test was poor in the Nigerian study. This may be explainable on the grounds that primary open-angle glaucoma and PACG were not differentiated.

Although our data suggest small differences between the performance of optical pachymetry in 1995 and 1997, examination of Figures 2, 3, and 4 suggests that the overall performance of the optical method is superior to that of handheld but not slitlamp US. Although there was no significant difference when the 2 US methods were compared, the AUC for slitlamp-mounted US was always greater. In the second phase (1997), 4 people operated the machine, replicating the likely scenario in a field-screening program involving a large team of staff. This will have introduced the possibility of interobserver variation, although the US machine we used is reported to give reproducible readings.

Although optical measurement and slitlamp US detected cases equally well, a greater proportion of sub-

DATA ANALYSIS

The shallower ACD of the 2 eyes was taken as the value for that subject. A subject was classified as an angle-closure suspect, or having PAC or PACG regardless of whether the features were present in one or both eyes. The units of analysis were therefore people, not eyes. The relationship between optical “true” ACD and age was summarized by means of the “lowess” procedure, which produces a robust smooth summary without imposing a regression model. The area under the curve (AUC) of a receiver operating characteristic plot was used as an index of global efficacy of the screening tests. The z test was used to assess whether the proportion of subjects correctly identified by 2 screening tests differed. Optical data were split according to year of examination for z test analysis, which requires completely independent or completely matched data. The predictive values of the test were calculated by means of the following prevalence rates: all occludable angles, 6.8%; PAC and PACG combined, 3.5%; and PACG alone, 0.8%. These figures apply to the population aged 40 years and older and are adapted from previously published studies to reflect the shift in emphasis of the term glaucoma, now used to denote people with optic neuropathy and visual loss. All analysis was carried out with proprietary software for personal computers (True Epistat; Epistat Services, Richardson, Tex). The lowess procedure was produced with SPSS statistical software (SPSS Inc, Chicago, Ill).
Subjects could not undergo measurement optically (4% vs 0.05%). As optical pachymetry requires expensive equipment and substantial training and is probably no better in practical terms than US, we confirmed our supposition that it is not a suitable screening tool. Handheld US is relatively easy to use and does not require a slitlamp, making it suitable for field use. The 2 US methods were similar in their abilities to detect occludable angles, although handheld US generated more false positives (Table 2). However, because of the higher number of false posi-

### Table 1. Details of Population, Sample Selected, and Cases Examined in Ömnögobi, Mongolia (1997)

<table>
<thead>
<tr>
<th>Center</th>
<th>Age, y</th>
<th>Men (Sample), No.</th>
<th>No. Examined</th>
<th>Women (Sample), No.</th>
<th>No. Examined</th>
<th>Total (Sample), No.</th>
<th>No. Examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalanzadgad</td>
<td>40-49</td>
<td>438 (70)</td>
<td>73*</td>
<td>433 (70)</td>
<td>107*</td>
<td>871 (140)</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>222 (70)</td>
<td>66</td>
<td>224 (70)</td>
<td>91*</td>
<td>446 (140)</td>
<td>157</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>187 (69)</td>
<td>50</td>
<td>192 (71)</td>
<td>61</td>
<td>379 (140)</td>
<td>111</td>
</tr>
<tr>
<td></td>
<td>≥70</td>
<td>119 (65)</td>
<td>54</td>
<td>145 (75)</td>
<td>51</td>
<td>264 (140)</td>
<td>105</td>
</tr>
<tr>
<td>Sevrei</td>
<td>40-49</td>
<td>75 (29)</td>
<td>29</td>
<td>91 (35)</td>
<td>35</td>
<td>166 (64)</td>
<td>64</td>
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<tr>
<td></td>
<td>50-59</td>
<td>38 (29)</td>
<td>28</td>
<td>46 (34)</td>
<td>35*</td>
<td>84 (63)</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>35 (24)</td>
<td>22</td>
<td>48 (35)</td>
<td>28</td>
<td>83 (59)</td>
<td>50</td>
</tr>
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<td></td>
<td>≥70</td>
<td>24 (14)</td>
<td>16*</td>
<td>61 (40)</td>
<td>29</td>
<td>85 (54)</td>
<td>45</td>
</tr>
</tbody>
</table>

* Oversampling occurred; see the “Results” section for explanation.

### Table 2. Performance of the 3 Tests in Detecting Occludable Angles, PAC and PACG Combined or PACG Alone

<table>
<thead>
<tr>
<th>Aiming to Detect All Cases of Test Used</th>
<th>No. of Subjects Examined</th>
<th>No. of Observations</th>
<th>ACD Cutoff, mm</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPVT</th>
<th>NPVT</th>
<th>Proportion of Cases Identified</th>
<th>Proportion of Normal Subjects Misidentified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occludable angles</td>
<td>Optical†</td>
<td>1717</td>
<td>1650</td>
<td>&lt;2.22</td>
<td>85</td>
<td>84</td>
<td>0.279</td>
<td>0.987</td>
<td>58/68</td>
</tr>
<tr>
<td></td>
<td>Slitlamp US</td>
<td>942</td>
<td>937</td>
<td>&lt;2.60</td>
<td>83</td>
<td>81</td>
<td>0.242</td>
<td>0.985</td>
<td>56/68</td>
</tr>
<tr>
<td></td>
<td>Handheld US</td>
<td>466</td>
<td>461</td>
<td>&lt;2.53</td>
<td>86</td>
<td>73</td>
<td>0.189</td>
<td>0.986</td>
<td>58/68</td>
</tr>
<tr>
<td>PAC and PACG combined</td>
<td>Optical†</td>
<td>1717</td>
<td>1650</td>
<td>&lt;2.21</td>
<td>84</td>
<td>82</td>
<td>0.145</td>
<td>0.993</td>
<td>29/35</td>
</tr>
<tr>
<td></td>
<td>Slitlamp US</td>
<td>942</td>
<td>937</td>
<td>&lt;2.60</td>
<td>84</td>
<td>79</td>
<td>0.127</td>
<td>0.993</td>
<td>29/35</td>
</tr>
<tr>
<td></td>
<td>Handheld US</td>
<td>466</td>
<td>461</td>
<td>&lt;2.53</td>
<td>73</td>
<td>68</td>
<td>0.076</td>
<td>0.986</td>
<td>26/35</td>
</tr>
<tr>
<td>PACG alone</td>
<td>Optical†</td>
<td>1717</td>
<td>1650</td>
<td>&lt;2.19</td>
<td>85</td>
<td>82</td>
<td>0.037</td>
<td>0.999</td>
<td>7/8</td>
</tr>
<tr>
<td></td>
<td>Slitlamp US</td>
<td>942</td>
<td>937</td>
<td>&lt;2.53</td>
<td>86</td>
<td>84</td>
<td>0.042</td>
<td>0.999</td>
<td>7/8</td>
</tr>
<tr>
<td></td>
<td>Handheld US</td>
<td>466</td>
<td>461</td>
<td>&lt;2.53</td>
<td>79</td>
<td>67</td>
<td>0.019</td>
<td>0.997</td>
<td>6/8</td>
</tr>
</tbody>
</table>

* PAC indicates primary angle closure; PACG, primary angle-closure glaucoma; ACD, anterior chamber depth; PPVT, positive predictive value of the test; NPVT, negative predictive value of the test; and US, ultrasound.
† Using prevalence figures quoted in the text.
‡ Optical data combined for 1995 and 1997.

Figure 1. Distribution of true optical anterior chamber depth (ACD) by age. Solid line represents mean age-specific ACD as estimated by loess curve. Crosses are cases of suspected primary angle closure; open circles, primary angle closure; and closed circles, primary angle-closure glaucoma. Small dots are the rest of the study population with ACD measurement.
tives with handheld US (252 vs 149 in screening 1000 individuals), slitlamp-mounted US again appears a more appropriate choice. Clearly, the cost and bulk of a slitlamp-mounted US system do not recommend it for field use in remote, rural areas. A successful compromise might incorporate a chin rest and forehead support with a stabilized US probe mounting, all of which could be clamped to a table.

If the US technique is to be successful in the field, reliability will be an important attribute. Instrument failure preventing examination of all subjects with the US device in 1997 highlighted a potential weakness. Further improvements in US accuracy may be possible. The resolution of ultrasound measurements depends on the frequency of the signal. Commercial A-mode ultrasound devices use a 10-MHz transducer to measure axial length, providing an axial resolution of 0.19 mm. A 50-MHz probe would improve anterior chamber resolution to 0.04 mm.

In implementation of a population-screening program, economic and logistic considerations must be borne in mind when the criterion of “test failure” is chosen. The choice of cutoff when screening for any condition is influenced by its prevalence, as this affects the predictive values of the test and determines the ratio of false-positive to true-positive results. For these reasons, it is an oversimplification to assume that optimal performance of the test is indicated by the point at which sensitivity and specificity are equal or closest; however, without data on the cost and benefits, we will assume that this is the case. Using an ACD of less than 2.60 mm measured by slitlamp-mounted US as the threshold for detecting occludable angles (prevalence, 6.8%) would give a predictive value of a positive test of 24%. Thus, in our study population, a test-positive subject will have a 0.24 probability, or 1 in 4 chance, of having an occludable angle. In practice, this would mean that screening 1000 subjects in our population would detect 56 of the 68 subjects with occludable angles and misidentify 149. If we seek to address glaucoma blindness by adopting a case-finding approach for PACG, the predictive power of a positive test would be much lower (0.042). This is because the low prevalence of PACG (0.8%) in our population generates poor predictive values even with good sensitivity and specificity. The burden of sorting out the diseased from healthy in the test-positive group is therefore much greater, 1 in 25 as opposed to 1 in 4. It would therefore only seem appropriate to screen for PACG by detecting occludable angles.

![Figure 2](https://archophth.jamanetwork.com/content/118/2/261){#fig2}

**Figure 2.** Receiver operating characteristic curve comparing optical pachymetry (diamonds) and slitlamp-mounted (triangles) and handheld (squares) ultrasound tests in the detection of occludable angles. The dashed line is the plot for a test with a predictive value equal to that of chance.

![Figure 3](https://archophth.jamanetwork.com/content/118/2/261){#fig3}

**Figure 3.** Receiver operating characteristic curve comparing optical pachymetry (diamonds) and slitlamp-mounted (triangles) and handheld (squares) ultrasound tests in the detection of primary angle closure and primary angle-closure glaucoma combined. The dashed line is the plot for a test with a predictive value equal to that of chance.
Although gonioscopy is the criterion standard for diagnosing an occludable angle, it is important to recognize that not all angles that look occludable will develop PACG. The proportion who develop PACG is difficult to estimate. Using different (broader) diagnostic criteria, Wilensky et al.12 found that persons with PACS had a 30% risk of developing an angle closure episode at 5 years. Ninety-four percent of that study’s subjects were white, and therefore extrapolation to our population is problematic. We believe the conversion rate may be higher in our population. A prospective study following subjects with occludable angles to determine the incidence of PACG would answer this question but this would be ethically complex. The current presumption that an unknown proportion progresses to disease is the basis for prophylactic iridotomy in PACS.

All test-positive individuals (and those in whom the test was not possible) require further assessment by a specialist. The people with false-positive results are in this way excluded from treatment. Prophylactic treatment would probably take the form of Nd:YAG laser iridotomy for all those with an occludable angle, which is consistent with current clinical opinion.28 Implementation of a screening program would require considerable resources, which would have to be considered when the cost-benefit ratio is calculated. It has been suggested that if a high-risk population (ACD < 1.8 mm) was identified and followed up for 5 years, and the incidence of PACG was 5% per year or greater, then one could consider prophylactic iridotomy on all of these people.29 We are not suggesting that all test-positive individuals should have prophylactic iridotomy without further assessment, but consideration may have to be given to it, if high costs otherwise prevent the implementation of a screening program. A further improvement in test validity may be obtained by subdividing by age and sex and assessing...
test performance. This would require a larger study than is presented herein to generate sufficient numbers.

In conclusion, we have confirmed the potential of ACD measurement as a screening tool for angle closure in this East Asian population and have discussed some of the problems faced when a screening program is implemented. We plan to perform a pilot screening trial with US in the near future to test the feasibility of population screening for PACG.

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