AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

Anterior Segment Imaging Predicts Incident Gonioscopic Angle Closure

Mani Baskaran, DNB,[1,2,3] *Jayant V. Iyer, MBBS, MMed,*[1] *Arun K. Narayanaswamy, DNB, MMed,*[1] *Yingke He, BSc(Hons),*[2] *Lisandro M. Sakata, MD, PhD,*[4] *Renyi Wu, MD, PhD,*[1,5] *Dianna Liu, MD,*[6] *Monisha E. Nongpiur, MD,*[1,2,3] *David S. Friedman, MD, PhD,*[6,*] *Tin Aung, FRCS(Ed), PhD*[1,2,3,*]

Purpose: To investigate the incidence of gonioscopic angle closure after 4 years in subjects with gonioscopically open angles but varying degrees of angle closure detected on anterior segment optical coherence tomography (AS OCT; Visante; Carl Zeiss Meditec, Dublin, CA) at baseline.

Design: Prospective, observational study.

Participants: Three hundred forty-two subjects, mostly Chinese, 50 years of age or older, were recruited, of whom 65 were controls with open angles on gonioscopy and AS OCT at baseline, and 277 were cases with baseline open angles on gonioscopy but closed angles (1−4 quadrants) on AS OCT scans.

Methods: All subjects underwent gonioscopy and AS OCT at baseline (horizontal and vertical single scans) and after 4 years. The examiner performing gonioscopy was masked to the baseline and AS OCT data. Angle closure in a quadrant was defined as nonvisibility of the posterior trabecular meshwork by gonioscopy and visible iridotrabecular contact beyond the scleral spur in AS OCT scans.

Main Outcome Measures: Gonioscopic angle closure in 2 or 3 quadrants after 4 years.

Results: There were no statistically significant differences in age, ethnicity, or gender between cases and controls. None of the control subjects demonstrated gonioscopic angle closure after 4 years. Forty-eight of the 277 subjects (17.3%; 95% confidence interval [CI], 12.8−23; $P < 0.0001$) with at least 1 quadrant of angle closure on AS OCT at baseline demonstrated gonioscopic angle closure in 2 or more quadrants, whereas 28 subjects (10.1%; 95% CI, 6.7−14.6; $P < 0.004$) demonstrated gonioscopic angle closure in 3 or more quadrants after 4 years. Individuals with more quadrants of angle closure on baseline AS OCT scans had a greater likelihood of gonioscopic angle closure developing after 4 years ($P < 0.0001$, chi-square test for trend for both definitions of angle closure).

Conclusions: Anterior segment OCT imaging at baseline predicts incident gonioscopic angle closure after 4 years among subjects who have gonioscopically open angles and iridotrabecular contact on AS OCT at baseline. *Ophthalmology 2015;■:1−5 © 2015 by the American Academy of Ophthalmology.*

See Editorial on page xxx.

Primary angle-closure glaucoma is a major cause of irreversible blindness in Asia, especially in people of Chinese ethnicity.[1,2] The reference standard for angle assessment remains gonioscopy, which requires topical anesthesia and a contact lens and is cumbersome and time consuming. In fact, nearly half of those with diagnosed glaucoma have no documentation of gonioscopy in the medical charts, indicating that there are barriers to carrying out the examination.[3] Anterior segment optical coherence tomography (AS OCT) is a noncontact technique for imaging the AS and iridocorneal angle and can be performed by a trained technician. We previously reported that AS OCT identified more eyes as having angle closure than gonioscopy.[4] Although this finding could indicate a high false-positive rate for AS OCT, it also could be the case that AS OCT is better able to identify milder forms of angle closure than gonioscopy because no external illumination is required and no contact is made with the eye, which can cause angle widening. Furthermore, there may be low iridotrabecular contact just above the scleral spur that can be seen as angle closure on AS OCT but would appear to be open on gonioscopy.[5] To determine whether those identified as closed on AS OCT have an increased risk of developing angle closure, we examined subjects with gonioscopically open angles but varying degrees of iridotrabecular contact as measured by AS OCT 4 years after the initial examination.

Methods

Study Population

The study was approved by the institutional review boards of the Singapore Eye Research Institute and Johns Hopkins University and adhered to the tenets of the Declaration of Helsinki. All subjects provided written informed consent. The primary study population consisted of phakic subjects 50 years of age or older who were examined in a community-based study of Singaporeans visiting a government-based polyclinic for nonophthalmic medical problems in 2007.[4] The study methodology and details of the study population have been described previously.[4]

http://dx.doi.org/10.1016/j.ophtha.2015.07.030
ISSN 0161-6420/15

A total of 2052 subjects completed all tests in 2007, and 1630 had open angles on gonioscopy. Of those with open angles on gonioscopy, 591 subjects (36.3%) had angle closure in 1 or more quadrants on AS OCT (defined as iris–trabecular contact beyond the scleral spur in any quadrant). For the current study, we examined 485 of 591 randomly selected individuals (82.1%; stratified by number of quadrants of AS OCT closure) with open angles on gonioscopy and angle closure in any quadrant on AS OCT (considered to be cases). We also examined a sample of subjects with open angles on both gonioscopy and AS OCT (considered the control group). The control group was chosen by computer-generated random selection from 738 of 1039 subjects (71%; with gonioscopic open angles with visible posterior trabecular meshwork in all quadrants, as well as open angles in all quadrants with reliable AS OCT scans) eligible from the baseline cohort.

After an initial interview about medical and ophthalmic history, all respondents underwent the following examinations on the same day: visual acuity, AS imaging by AS OCT in the dark (Visante AS OCT; Carl Zeiss Meditec, Dublin, CA), and anterior chamber depth (ACD) and axial length (AL) measurements (IOLMaster, software version 3.02; Carl Zeiss Meditec) by a single operator. The AS OCT and IOLMaster hardware and software versions were the same at baseline and at the 4-year follow-up study. Goldman applanation tonometry, gonioscopy (details below), and optic disc assessment using a 78-diopter (D) lens by slit-lamp biomicroscopic examination were performed. Individuals were excluded at baseline and follow-up if they had a history of intraocular surgery, previous AS laser treatment, or penetrating trauma to the eye. In addition, those with aphakia or pseudophakia on examination as well as those with corneal disorders that could influence imaging by AS OCT, such as corneal endothelial dystrophy, corneal opacity, or severe pterygium, were excluded.

Anterior Segment Optical Coherence Tomography Imaging

Imaging with AS OCT was performed in dark room conditions (0 lux) by a single operator who was masked to the results of all the other tests performed. The standard AS single-scan protocol, which produces 256 scans in 0.125 seconds, was used, and scans were centered at the pupil. To obtain the best-quality image, the examiner adjusted the saturation and noise and optimized the polarization for each scan during the examination. The examiner chose the best image with the least motion or image artifacts resulting from the eyelids, masked to the patient's clinical data, including gonioscopic and baseline imaging results. Similar lighting conditions, scan protocols, and analyses were used for baseline and follow-up visits.

A glaucoma fellowship–trained ophthalmologist (L.M.S.) assessed all AS OCT images (both at baseline and after 4 years), masked to gonioscopic and AS OCT findings, to determine the number of quadrants that were open or closed based on presence of iridotrabecular contact. Baseline and follow-up AS OCT images were assessed over 2 different sessions to avoid bias.

Gonioscopy

Gonioscopy was performed in the dark in all cases by a single examiner (M.B.) masked to AS OCT findings. Nonindentation gonioscopy was performed using a Goldmann 2-mirror lens (Ocular Instruments, Inc., Bellevue, WA) at high magnification (×16) with the eye aligned to the goniolens in the primary gaze position. Care was taken to avoid light falling on the pupil. Indentation gonioscopy also was performed using a Sussman 4-mirror lens (Ocular Instruments, Inc.). The angle in each quadrant was graded based on the anatomic structures observed during gonioscopy (grade 0 = no angle structures, grade 1 = Schwalbe's line, grade 2 = anterior trabecular meshwork, grade 3 = posterior trabecular meshwork or scleral spur, grade 4 = visible ciliary body). This grading system was derived from the modified Scheie's angle grading system.[6] A quadrant was considered to be closed if the posterior trabecular meshwork could not be seen in the primary position without indentation (grade 0, 1, or 2). Gonioscopic angle closure in an eye was defined as closure in 2 or more quadrants.

Measurements of the Other Ocular Variables

A trained ophthalmic technician measured the ACD and AL with the IOLMaster. The IOLMaster measures ACD from the corneal epithelium to the anterior lens surface with lateral slit illumination. The averages of 5 readings obtained for ACD and AL, and 3 consecutive readings obtained for corneal curvature, were calculated and used for subsequent analyses. All readings for each parameter were required to be within 0.05 mm of the reading within the highest signal-to-noise ratio. Goldmann applanation tonometry was used to measure intraocular pressure (IOP), and the vertical cup-to-disc ratio was determined clinically using a 78-D lens at the slit lamp with a graticule (Haag-Streit Model BQ-900; Haag Streit, Koeniz, Switzerland). The median of 3 IOP readings was used for analysis. All clinical measurements were performed by a glaucoma fellowship–trained ophthalmologist (M.B.) masked to the baseline and follow-up AS OCT findings.

Statistical Analysis

Statistical analyses were performed using SPSS software version 18.0 for Windows (SPSS, Inc., Chicago, IL). Demographic and clinical parameters at the baseline evaluation between the participants and nonparticipants were compared with the t test for continuous variables and the chi-square test for categorical variables. The incidence of angle closure on gonioscopy and the association between incident angle closure and baseline AS OCT findings were compared using the Fisher exact test and the chi-square test for trend. Statistical significance was found at $P < 0.05$.

Results

Demographics

Telephone calls were made to a total of 585 subjects, of whom 53 were ineligible (23 underwent bilateral cataract surgery during the follow-up period and 30 had medical conditions such as stroke and heart attack that prevented them from coming for the examination) and 12 had died. Of the remaining 520 subjects, 342 (65.8%) responded and were able to make a follow-up visit, 118 (22.8%) declined to come in for a follow-up visit, and 60 (11.6%) subjects could not be contacted (Fig 1). Two hundred seventy-seven of the 342 responding subjects were considered cases (having 2 or more angles closed on baseline AS OCT), whereas 65 were controls.

Of the eligible subjects, men (59.7% vs. 40.3% women; $P = 0.003$) were less likely to participate, as were older individuals. Participants and nonparticipants were similar in ethnicity and baseline ocular clinical parameters such as AL, ACD, IOP, and mean gonioscopic grading (Table 1). There were also no statistically significant differences in baseline age, ethnicity, gender, spherical equivalent, visual acuity, and IOP between participating cases and controls, whereas cases had shorter AL and ACD (Table 2).