

Diagnostic Tools for Primary Angle Closure

Beyond relative pupillary block—identifying alternative mechanisms for primary angle closure with advanced technology.

BY JASON A. GOLDSMITH, MD, MS

Diagnostic tools for the detection of primary angle closure include old stalwarts such as gonioscopy and slit-lamp estimation of limbal anterior chamber depth^{1,2} as well as new technologies that yield high-resolution, cross-sectional images of the angle. In addition to their diagnostic potential, anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM) have provided insight into newly identified mechanisms of primary angle closure that go beyond the effect of relative pupillary block. These etiologic insights may enhance diagnostic accuracy, prognostication, and treatment selection. Other imaging modalities, including Scheimpflug photography¹ and the scanning peripheral anterior chamber depth analyzer,³ are currently under investigation but do not provide direct images of the angle recess.

GONIOSCOPY, AS-OCT, AND UBM

Gonioscopy is the most comprehensive diagnostic tool for angle closure. It can assess the angle/iris relationship,

distinguish between appositional and synechial closure, and provide visualization of the double-hump sign of plateau iris and the vessels of neovascular angle closure. In uncertain diagnoses, gonioscopy can provide visual clues to the presence of pigment dispersion, pseudoexfoliation, and elevated episcleral venous pressure. It is unlikely that novel imaging technology will replace gonioscopy for many of these essential functions.

Gonioscopy, however, is subject to light-induced miosis and inadvertent corneal compression, artifacts that are capable of unintentionally opening the angle. In addition, because gonioscopy can be difficult to master and interpret, its results may be diagnostically uncertain. Gonioscopy is therefore often neglected, potentially resulting in misdiagnosis. For these reasons, among others, alternative imaging technologies are attractive.

The advantages of AS-OCT include that it is noncontact and does not require a highly skilled technician. Upon the identification of the scleral spur with AS-OCT (or UBM)

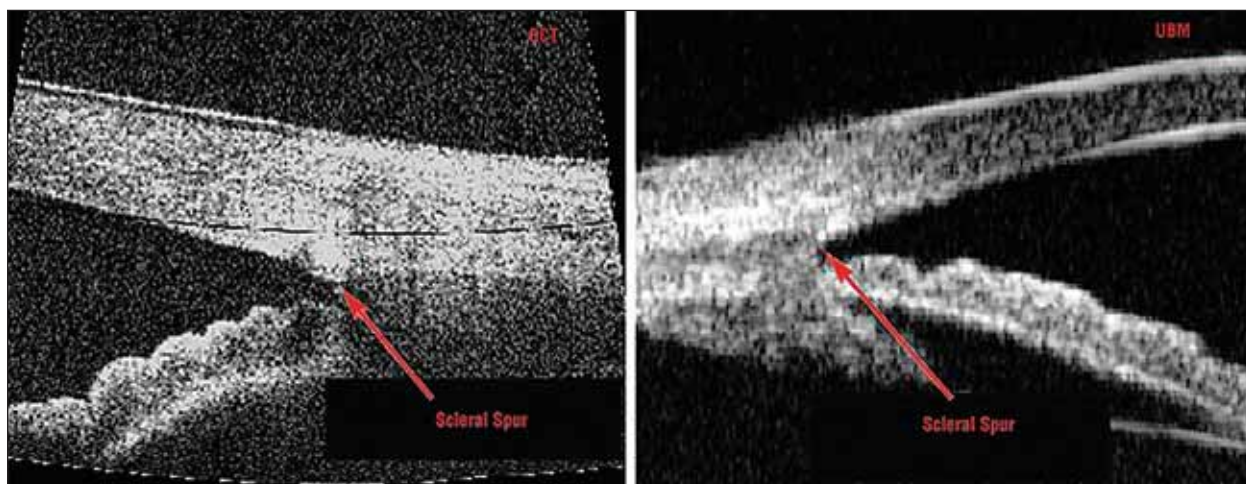


Figure 1. Side-by-side comparison of an OCT image and UBM image of the anterior chamber angle obtained from a single subject. (Reprinted with permission from Arch Ophthalmol. 2005;123(8):1053-1059. ©2005 American Medical Association. All rights reserved.)

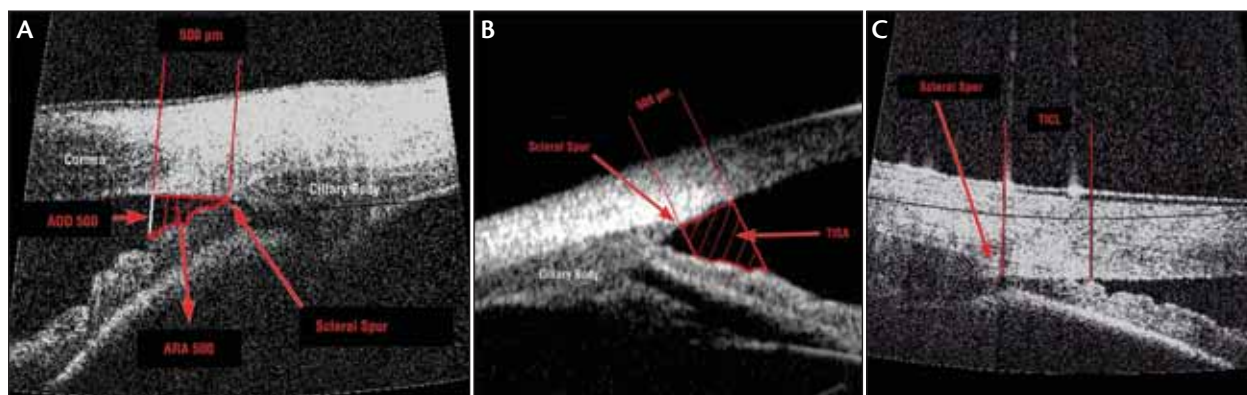


Figure 2. Angle opening distance at 500 μm (AOD 500) and angle recess area at 500 μm (ARA 500) depicted on an OCT image of a lightly pigmented eye. Note that the ARA follows the iris contour (A). Trabecular-iris space area (TISA) at 500 μm measured on a UBM image of a subject with a deep angle recess. Note that the area behind the scleral spur is not included in the TISA (B). Trabecular-iris contact length (TICL) depicted on an OCT image of a subject with narrow angles on gonioscopy (C). (Reprinted with permission from Arch Ophthalmol. 2005;123(8):1053-1059. ©2005 American Medical Association. All rights reserved.)

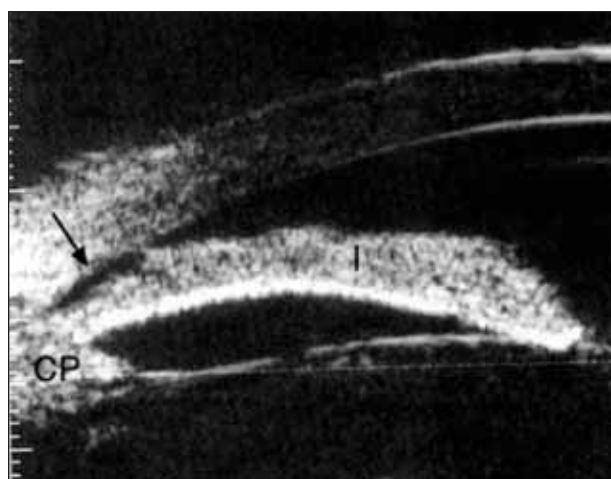


Figure 3. UBM image in a case of pupillary block preiridotomy. The iris (I) shows anterior bowing indicating a pressure differential between the posterior and anterior chambers. The angle is narrow (arrow), and the ciliary sulcus is open. CP = ciliary process. (Reprinted from Mandell MA, Pavlin CJ, Weisbrod DJ, Simpson ER. Anterior chamber depth in plateau iris syndrome and pupillary block as measured by ultrasound biomicroscopy. Am J Ophthalmol. 2003;136(5):900-903, with permission from Elsevier. ©2003.)

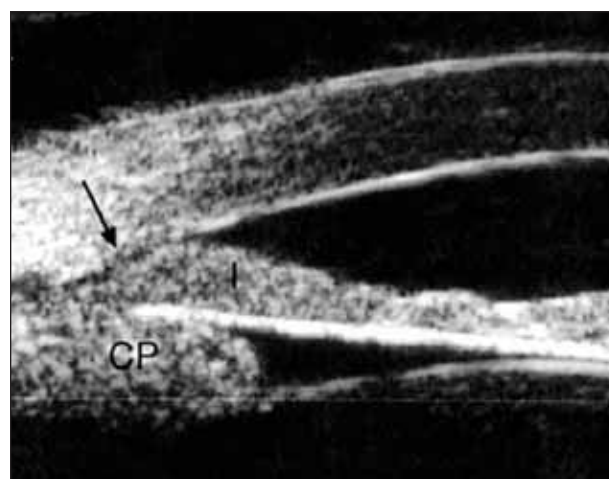


Figure 4. UBM image in a case of plateau iris syndrome postiridotomy. This image demonstrates a nonpupillary block mechanism in which forward positioning of the ciliary processes (CP) closes the peripheral angle (arrow) despite a flat iris profile (I). (Reprinted from Mandell MA, Pavlin CJ, Weisbrod DJ, Simpson ER. Anterior chamber depth in plateau iris syndrome and pupillary block as measured by ultrasound biomicroscopy. Am J Ophthalmol. 2003;136(5):900-903, with permission from Elsevier. ©2003.)

(Figure 1), various iridocorneal angle parameters can be measured (Figure 2). Potential benefits include efficient population screening in order to identify individuals at risk for angle closure, although this capability remains unproven. AS-OCT cannot penetrate posterior to the iris.

UBM, in contrast, penetrates deep enough to image the ciliary body (Figures 1, 3, and 4). The main drawbacks of UBM are that it must be performed by a skilled technician and that direct contact may alter the angle's

width. The benefits of UBM include its utility in identifying nonpupillary block mechanisms for angle closure—mechanisms that may contribute to angle closure in the majority of Asian patients.⁴

Both UBM and AS-OCT can identify narrow and closed angles with reasonable performance.⁵ Neither, however, can reliably differentiate between appositional and synechial closure, an essential distinction prior to surgical intervention. As discussed later, the lack of a

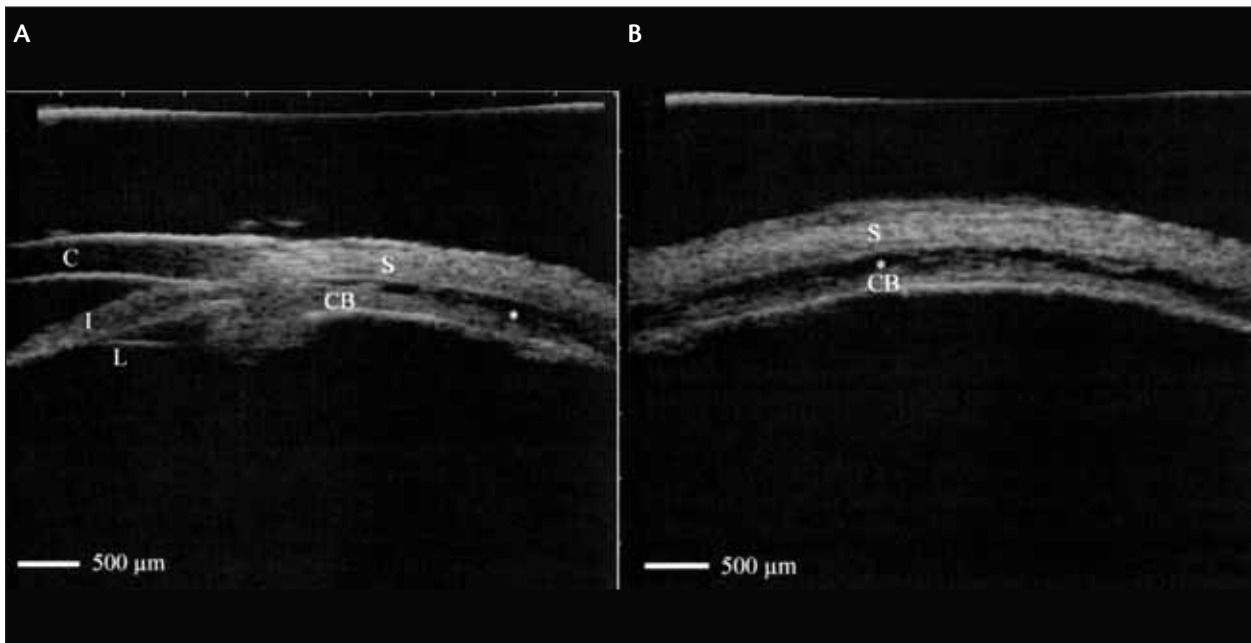


Figure 5. Radial (A) and transverse (B) sections of UBM findings of a 44-year-old female's eye with acute primary angle-closure glaucoma. IOP was 44 mm Hg at initial examination and was successfully reduced to 12 mm Hg on the next day. Grade 3 uveal effusion (*) was evident as a hypoechoic area between the sclera (S) and the pars plana of the ciliary body (CB) on the next day. Note the angle was still closed. C = cornea; I = iris; L = lens. (Reprinted with permission from Sakai H, Morine-Shinjo S, Shinzato M, et al. Uveal effusion in primary angle-closure glaucoma. *Ophthalmology*. 2005;112(3):413-419. ©Elsevier 2005.)

TABLE 1. CLASSIFICATION SYSTEMS FOR PRIMARY ANGLE CLOSURE

AAO Preferred Practice Pattern ¹³	Research Definition ¹⁵	Symptom-Based System ¹⁵
Anatomic narrow angle (PAC suspect): the peripheral iris is located close to, but does not touch, the posterior pigmented trabecular meshwork	Primary angle-closure suspect: ITC in three or more quadrants ^a ; normal IOP; disc, field; no evidence of PAS	Acute: abrupt onset, symptomatic, elevated IOP that is generally not self-limiting
Primary angle closure: narrow/closed angle plus evidence including elevated IOP, PAS, sector iris atrophy, or glaukomflecken. Can be acute, intermittent, or chronic	Primary angle closure: ITC in three or more quadrants with raised IOP and/or primary PAS. Disc and field are normal	Subacute/intermittent: abrupt onset, symptomatic, elevated IOP that is self-limiting and recurrent
Primary angle-closure glaucoma: PAC plus glaucomatous optic neuropathy	Primary angle closure glaucoma: ITC in three or more quadrants with raised IOP and/or primary PAS, plus disc and field evidence for glaucomatous optic neuropathy	Chronic: elevated IOP or PAS resulting from angle closure that is asymptomatic

Abbreviations: PAC, primary angle closure; PAS, peripheral anterior synechiae; ITC, iridotrabecular contact.

^aControversy exists with respect to the number of quadrants of ITC necessary to define a PAC suspect, with some physicians advocating as few as one quadrant of ITC.

validated classification system containing a clear case definition for occludable angles prevents predicting which narrow angles are at significant risk of closure. Finally, the identification of the scleral spur can be ambiguous for both UBM and AS-OCT. Without the localization of this landmark, diagnostic uncertainty may remain.⁶

NONPUPILLARY BLOCK MECHANISMS FOR ANGLE CLOSURE

Nonpupillary block mechanisms include plateau iris, traditionally described as a steep peripheral iris prone to closure and refractory to laser peripheral iridotomy. Plateau iris appears to occur secondary to anterior rotation of the ciliary processes—a UBM finding—which results in buttressing of the peripheral iris against the trabecular meshwork (compare Figure 3 to Figure 4). Another UBM finding is the loss of the ciliary sulcus. Other anatomical variants

“A primary goal of research on ocular biometry with respect to primary angle closure is the development of a predictive model that forecasts the likelihood of developing angle closure.”

that appear to predispose eyes to nonpupillary block mechanisms include prominent peripheral iris roll and variability in iris insertion.^{1,4}

Another potential nonpupillary block mechanism is uveal effusion, a UBM finding that has been associated with 25% of acute primary angle closure cases in Asian eyes (Figure 5).⁷ An intriguing hypothesis describes the potential contribution of choroidal expansion and result-

DISCUSSION: CLASSIFICATIONS IN CONTEXT

BY MARC F. LIEBERMAN, MD

In the article by Jason A. Goldsmith, MD, MS, it is interesting to see the three available schemes for classifying angle-closure glaucoma (ACG) in tabular form. One must recognize, however, that these systems are not of equivalent worth and, in fact, are historically sequential.

The “symptom-based” scheme is the oldest. The system was cobbled together from clinical observations made since Curran’s emphasis on “chronic” and “acute” glaucomas in Europe in the 1930s. It was refined by Barkan’s distinction between open- and closed-angle glaucoma, endorsed by the AAO in 1949.¹ Except for acute presentations of ACG, the adjectival emphasis on the presumed time course of the condition (eg, “intermittent” or “subacute”) is based on subjective information and is of dubious value. Nevertheless, temporal descriptions have persisted in textbooks until the last decade, qualified by primary and secondary designations and amplified by elaborative descriptions of the pushing and pulling mechanisms underlying the various clinical presentations.²⁻⁵

This older nomenclature of *chronic* and *acute* ACG (still enshrined in ICD coding) is too imprecise for clinicians or researchers to systematically compare patients, outcomes, or prognoses. In 2005, the authors of the AAO’s *Preferred Practice Patterns* suggested three categories of (1) narrow angle (vaguely defined), (2) angle closure (still retaining time-based terminology), and (3) frank glaucomatous damage resulting from impaired outflow. Clinicians never widely embraced this classification system, which is handicapped by the absence of parameters for quantifying the extent of trabecular compromise.

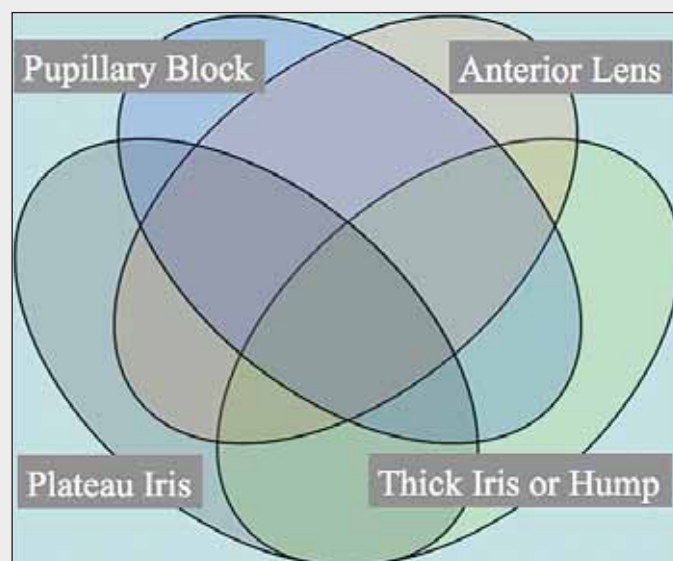


Figure 1. The possible overlapping mechanisms underlying the presentations of ACG. (Modified with permission from S. Radhakrishnan, MD.)

After years of epidemiologic refinement, an international consensus for more robust definitions was reached in 2006 by the Association of International Glaucoma Societies⁶ and subsequently endorsed by the AAO and other international ophthalmic organizations. Although Dr. Goldsmith refers to these classifications as *research definitions*, I would contend that they are in fact superbly applicable to clinical management: they are both practical and easy to adapt to the routine care of patients.⁷

ant posterior pressure to the etiology of angle closure in some cases.^{8,9}

PREDICTIVE MODELS

A major goal of research on ocular biometry with respect to primary angle closure is the development of a predictive model that forecasts the likelihood of developing angle closure, thus providing guidance as to when to intervene surgically. Biometric variables that are potentially correlated with the risk for angle closure include anterior chamber depth, axial length, and the lens' thickness as well as UBM- and OCT-measured angle parameters and the nonpupillary block factors discussed earlier. Future predictive models may also include biometric variables with demographic risk factors (eg, age, race, gender).

Despite extensive investigation into such biometric parameters, the predictive capability of current models is limited.¹⁰ Only approximately 10% to 25% of untreated

primary angle-closure suspects will develop angle closure.^{9,10} Without reliable prognostic indicators from clinical examination or biometry, it is uncertain which primary angle-closure suspects require treatment. Two large clinical trials of these suspects—one in Guangzhou, China,¹¹ and one in Singapore¹²—should provide useful information regarding prognostic risk factors, the natural history of untreated eyes, and the efficacy of treatment. These studies have a similar design in which one eye is randomized to laser peripheral iridotomy and the other is followed without treatment.

CLASSIFICATION SYSTEMS

The major differences between several available classification systems for primary angle closure (Tables 1 and 2) are whether (1) a suspect is defined by the degree of the angle's narrowness or by appositional closure, (2) symptoms are considered, and (3) the underlying mechanism(s)

In this classification system, an eye that presents with some form of ACG is defined entirely on the basis of the clinical examination, without reference to symptoms or history. Using indentation gonioscopy and other clinical data, the clinician discriminates between the three disease stages:

- A primary angle-closure suspect (PACS) has an *angle at risk*, with 270° of iridotrabecular contact (The requirement for 75% iridotrabecular contact is the current, "high-threshold" definition, but a lower threshold of 50% has been used in some studies.⁸)
- Primary angle closure (PAC) signifies an *angle with damage*, either structural (peripheral anterior synechiae) or functional (elevated IOP)
- Primary angle-closure glaucoma (PACG) represents a *damaged angle with optic neuropathy*—disc cupping and/or visual field loss

Upon determining the disease stage, the clinician's search begins for the responsible mechanism(s). Note the use of the plural: more than one set of anatomic configurations can be at play (Figure 1). For example, laser iridotomy does not deepen the angles of approximately one-third of the eyes with suspected primary angle closure. Mechanisms other than pupillary block, such as plateau iris or angle crowding from an anteriorly positioned cataract, may be responsible. Ultrasound biomicroscopy and anterior segment optical coherence tomography are invaluable for determining mechanisms.

Because clinical provocative tests have uniformly failed in prospective randomized studies to predict a particular eye's clinical trajectory, the best clinicians can do for now is to extrapolate from their stage-specific classification of an eye (eg, primary angle closure) and to incorporate other known risk factors (eg, elderly

Chinese female) when deciding whether to observe or intervene. By universally adopting the new quantitative and evidence-based classification of ACG, it is to be hoped that physicians can integrate future prospective studies regarding stage-specific treatments and outcomes into the care of their patients. □

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TABLE 2. PARALLEL CLASSIFICATION OF STAGE AND MECHANISM OF PRIMARY ANGLE CLOSURE*Disease staging*

Stage 1: Narrow angle (angle-closure suspect)—an anatomical predisposition to closure.

Stage 2: Angle closure—Partial or total closure of the angle with synechiae and /or raised IOP (height and cumulative circumference of PAS should be recorded). (a) Non-ischaemic; (b) ischaemic—with tissue injury such as iris whorling or stromal atrophy, often history of symptoms.

Stage 3: Angle closure with glaucomatous optic neuropathy.

Mechanism of closure

A. Pupil block.

B. Anterior non-pupil block—including plateau iris and peripheral iris crowding.

C. Lens-related.

D. Factors behind the lens.

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for angle closure are considered.

The AAO's *Preferred Practice Pattern for Angle Closure* advocates a diagnostic scheme that defines primary angle closure suspects as having narrow but not closed angles.¹³ The Academy's position is that "laser iridotomy may be considered for patients with narrow angles who require repeated pupil dilation for treatment of other eye disorders." In contrast, a widely used research definition developed by Foster and colleagues¹⁴ defines primary angle-closure suspects as having at least three quadrants of apposition of the iris to the trabecular meshwork but without peripheral anterior synechiae, elevated IOP, or the other factors shown in Table 1. The rationale behind this system is that patients with up to three quadrants of apposition can probably be observed without treatment. Again, the results from the two major clinical trials described earlier should provide clarification.

It is no longer satisfactory to use the older, primarily symptom-based clinical classification system consisting of acute, subacute/intermittent, and chronic angle-closure categories. This scheme has little or no prognostic value, does not guide management, and does not distinguish between elevated IOP and glaucomatous optic neuropathy¹⁵ (Table 1). A more comprehensive approach advocates using a stage-based system in combination with a mechanism-based system⁴ (Table 2).

STATIC VERSUS DYNAMIC BIOMETRIC PARAMETERS

Much of the research to date on diagnostic tools for primary angle closure has focused on static biometric

parameters. Researchers are beginning to recognize that many important parameters are dynamic and subject to physiologic fluctuation, including pupillary dilation and its recently described relationship to iris volume. Specifically, normal eyes have peripheral irides that thin with dilation, but AS-OCT analysis has demonstrated that the iris thins to a lesser degree with dilation in eyes that have primary angle closure.^{9,16} An additional, potential, dynamic physiological factor is choroidal swelling.^{8,9} Future predictive models may include dynamic variables, which may have a greater impact on forecasting the risk for angle closure than the static variables studied to date. □

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