Editorial Commentary

Assessment of angle width using anterior segment optical coherence tomography

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Introduction

Primary angle closure glaucoma (PACG) accounts for nearly half of glaucoma related blindness in the world with majority occurring in Asian populations (1,2). A range of phenotypes are recognized within the spectrum of primary angle closure disease (PACD), namely primary angle closure suspects (PACS, occludable angles with normal intraocular pressure and optic disc), primary angle closure (PAC, occludable angles with features indicative of trabecular outflow obstruction or raised intraocular pressure but absence of glaucomatous optic neuropathy) and finally PACG (presence of glaucomatous optic neuropathy) (3). Angle assessment plays an important role in the diagnosis and management of PACD. Traditionally the diagnosis is established using gonioscopy. Though to date gonioscopy remains the gold standard technique for angle assessment, it is not without limitations. Gonioscopy is a highly subjective procedure and interpretation can vary based on the skill and experience of the examiner performing this procedure leading to intra and inter-observer discrepancies. Additionally, the results and accuracy of gonioscopic examination can vary drastically as a result of changes in illumination which can falsely open the anterior chamber angle (ACA) as well as patient cooperation and direction of gaze.

With the advances in technology it is now possible to perform objective, reproducible, high resolution imaging of the ACA using devices such as high frequency ultrasound biomicroscopy (UBM), Scheimpflug imaging system, and anterior segment optical coherence tomography (AS-OCT). These imaging techniques help us to understand the pathophysiology of angle closure in a better way. Compared to UBM, AS-OCT achieves higher resolution and does not require contact with the ocular surface. AS-OCT is a noncontact, rapid imaging device that uses low-coherence interferometry to obtain cross-sectional images of the anterior segment (4). The measurements obtained from AS-OCT are semi-automated, reproducible (5,6) and unlike gonioscopy these measurements are operator independent. The swept source OCTs (SS-OCT), such as the Tomey CASIA SS-1000 (Tomey corporation, Nagoya, Japan), utilize a laser wavelength of 1,310 nm and employ scan speed of 30,000 A-scans/s with an axial resolution of 10 µm. SS-OCTs have recently become commercially available and are able to capture extremely high-resolution images.

All automated biometric analyses of the AC angle using AS-OCT require a reference landmark from which the angle measurements are derived. Typically, the scleral spur is used as a reference point for parameters such as the iris area and volume, angle opening distance (AOD), angle recess area, scleral thickness, trabecular meshwork-ciliary process distance, trabecular iris angle (TIA), and trabecular iris space area (TISA). The other possible biometric measurements include iris thickness (IT), iris curvature (IC), anterior chamber depth (ACD), anterior chamber width (ACW), and lens vault (LV). As the location of the SS must be manually determined, this introduces some level of intra and inter-observer variability to these imaging techniques. Additionally, the location of the SS is not always apparent, especially when image quality is poor, resulting in

potential inaccuracies and limiting the utility of automated segmentation softwares.

AS-OCT *vs.* Gonioscopy

The performance of AS-OCT has been compared with the gold standard gonioscopy in various studies. Nolan *et al.* reported that AS-OCT had a high sensitivity of 98% in diagnosing angle closure as compared to gonioscopy. However, the specificity was only 44.6% (7). Similarly various other studies have shown that the AS-OCT has a high sensitivity and low to moderate specificity in screening for angle closure suggesting some eyes with gonioscopically open angles are being falsely categorized as having angle closure on AS-OCT (8). Chang *et al*. demonstrated that the specificity of detecting angle closure with AS-OCT could be improved significantly to 94.3% by combining it with peripheral ACD analyzer (9). Though it is possible that AS-OCT may be detecting sub-clinical stages of angle closure as Baskaran *et al*. found that eyes with more quadrants of angle closure on AS-OCT at baseline had a greater risk of angle closure on gonioscopy in the next 4 years (10). They also found that the subjects who had open angles on AS-OCT at baseline did not develop gonioscopic angle closure during follow up. These findings support the idea that the AS-OCT imaging may be able to predict the incident angle closure on gonioscopy. Despite gonioscopy being the gold standard intra-observer variability had been found to be better for AS-OCT (11).

ACA width

The key anatomic parameter that determines the risk of angle closure disease is the width of the anterior chamber angle determined with gonioscopy. PACD is common in eyes which have shallow anterior chamber (determined by central anterior chamber depth or ACD), shorter axial length (AL), and thick, anteriorly positioned lens (12,13). Among these factors shallow ACD is one of the most important factor and it is the only factor which can be assessed using a routine slit lamp examination. But studies have suggested that only a small proportion of subjects with shallow ACD progress and develop angle closure disease (14). Recent AS-OCT based studies have shown that eyes with gonioscopically narrow angles have thicker irides with greater iris curvature (15), shorter ACW (16), smaller ACA and anterior chamber volume (ACV) (17), and greater LV suggesting other features may be equally or more important (18).

Commentary

Previous studies have shown the role of various biometric features associated with angle closure, defined by AS-OCT. But the relative and unique contributions of the various anatomical structures to decreased angle width with AS-OCT remains unclear. In their article in American Journal of Ophthalmology, Xu *et al*. have assessed the contributions of various ocular biometric features to AS-OCT determined angle width in a large population based study of Chinese Americans, 50 years or older participating in the Chinese American Eye Study, CHES (19). The authors chose AOD 750 and TISA 750 to represent the angle width as evidence suggests that these two parameters correlate well with gonioscopic angle closure and elevated intraocular pressure respectively.

Though they used SS-ASOCT to image the anterior chamber angle, the authors used a single image from the temporal quadrant from one eye of each individual to develop model predicting temporal quadrant measurements of angle width (AOD 750 and TISA 750). In development of such models accounting of collinearity of parameters is of great importance. As such the authors used separate multivariable models to evaluate the contributions of LV and ACD to angle width as these parameters were highly collinear. Similarly, AL was excluded in favor of its components [ACD, vitreous cavity depth (VCD), lens thickness (LT)] due to high collinearity with VCD.

Contribution of each independent parameter was then estimated using the magnitude of standardized regression coefficients (SRCs) and semi-partial correlation coefficients squared (SPCC2s) both of which rely on R2 statistics, while accounting for age and sex. While univariable models demonstrated significant association of all independent biometric parameters with angle width, multivariable models showed that ACD, LV, and IC were the strongest determinants of angle width. Though anterior chamber area (ACAr) and ACV were not included in this analysis unlike prior publication by Foo *et al*. (20), the estimated R2 for contribution of ACD, LV and IC to angle width in the two studies are in close agreement.

These findings are in accordance with known mechanisms of angle closure disease. For example ACD is used widely in screening efforts of PACD and has been shown to be closely related to progression from gonioscopically open to closed angles in multiple populations (21-23). Similarly, the contribution of LV is not surprising as this parameter is greatly influenced by LT and

ACD. LT has been similarly associated with progression in AC eyes (23). IC is likely a more dynamic parameter that is associated with greater degree of pupillary block and indeed has been shown to decrease after laser iridotomy (24).

Gonioscopy remains the gold standard in diagnosis and management of PACD. AS-OCT has excellent sensitivity and a moderate specificity to detect narrow angles as compared to gonioscopy. Various quantitative and qualitative parameters have shown good agreement with gonioscopically closed angles (25). Sequential testing helps to assess the progression of angle closure. It helps us to understand the pathophysiology of acute primary angle closure. The effects of various treatment modalities including laser iridotomy and lens extraction can be assessed quantitatively using AS-OCT. With the development of SS-OCT, now it is even possible to quantify peripheral anterior synechiae and to discriminate synechial from appositional angle closure. There is increasing evidence that AS-OCT may be a more objective and accurate method of following such eyes and developing models that can determine angle width as is done in this study and more importantly accurately predict progression to glaucoma and high eye pressure would be revolutionizing for the field.

Strengths and limitations

One of the unique features of this study is that it was designed to explore the relative and unique contributions of ocular structures and biometric parameters to angle width using both SS-OCT and A-scan biometry. Factors which can influence the angle width including medications, laser procedures, and intraocular surgeries were carefully excluded.

We need to remember that the study population consisted of only Chinese Americans and hence we cannot generalize the results to other ethnicities. Marking the scleral spur is an important step to assess various parameters with AS-OCT. Only one observer was utilized to mark the spur, making the study less pragmatic, as there is no room to assess inter-observer variability. Additionally, IT has been shown in multiple studies as an important predictor of angle width, but unfortunately it was not captured in this study.

Conclusions

Gonioscopy still remains the gold standard for angle assessment. However, AS-OCT is emerging as a promising quantitative tool for assessment of the angle width. Studies such as this, allow us to understand the contributions from various parameters and shed light on the mechamisms of angle closure. A better understanding of these factors will aid clinical decisions on the management of angle closure in the form of a laser iridotomy or a lens extraction based on the major contributing factors. However, we need to remember that apart from these anatomical parameters, physiological and dynamic factors play a role in angle closure. Importantly, there is a need to explore the role of various anatomic factors in other ethnicities.

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