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Review article

Clinical application of anterior segment optical coherence tomography for angle-closure related disease

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A B S T R A C T

Anterior segment optical coherence tomography has the ability to acquire angle-to-angle cross-sectional anterior chamber images in a non-contact way, and this technology shows a good reproducibility for angle parameters. With the availability of image processing software, some novel anatomic parameters such as iris area, iris volume, anterior chamber area, anterior chamber volume, anterior chamber width, and lens vault have been evaluated for the diagnosis of angle-closure related disease. This review article will describe the definitions of these interior segment optical coherence tomography parameters and summarize recent findings about these parameters in diagnosing angle-closure disease.

1. Introduction

Primary angle-closure glaucoma (PACG) is a leading cause of blindness in the world, especially in Asia.[1,2] Diagnosis and treatment are highly related to angle assessment techniques. Traditionally, diagnosis of PACG is based on the findings of gonioscopy. However, the gonioscopic examination needs an experienced ophthalmologist using a slit lamp and a gonioscopic lens to do the test well. It should be performed under dark conditions, minimizing light through the pupil. Also, the patient's cooperation is quite important to get a good-quality examination result since the examination is done with a contact approach. Due to the above reasons, this method is not suitable for massive screening. A-scan sonography to measure central anterior chamber depth (ACD), lens thickness (LT), and ocular axial length (AL) has been studied as an alternative method to screen PACG. In previous studies using A-scan sonography to measure ocular parameters, investigators found that shallow central ACD, increased LT, and short AL are risk factors for having angle-closure glaucoma.[3–5] Using this technology, lens position (LP; defined as ACD + 1/2 LT), relative RLP (defined as LP/AL), and LT/AL ratio have been evaluated to diagnose angle-closure glaucoma. However, conflicting results on the importance of these calculated lens-related parameters with angle-closure glaucoma have been reported.[6–9]

However, A-scan sonography cannot assess the anterior chamber angle directly; it measures surrogate ocular parameters to assist in the diagnosis of angle-closure related disorders. Imaging technologies which could provide cross-sectional angle pictures is more helpful for diagnosing angle-closure related disease. Ultrasound biomicroscopy (UBM) and anterior segment optical coherence tomography (ASOCT) are two popular methods that could acquire cross-sectional angle images and allow quantitative measurement of angle, iris, and anterior chamber parameters.

Although ASOCT is not able to acquire images behind iris tissue like UBM can, it can scan angle to angle within one scan with good visualization of the angle recesses. In addition, ASOCT can acquire images under dim conditions and is performed in a non-contact fashion. All of these characteristics make ASOCT more popular for anterior chamber angle evaluation.[10,11] This article will focus on the anatomic parameters acquired by ASOCT and results of recent studies using ASOCT for the diagnosis of angle-closure glaucoma.

2. Definitions of ASOCT parameters

Some anatomic parameters such as angle opening distance (AOD), angle recess area (ARA), and trabecular-iris space area (TISA) were developed in the era of UBM; these parameters measured by ASOCT follow the definitions used in UBM. Since ASOCT cannot

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image the structures behind the iris, ASOCT is not able to measure iris ciliary process distance and trabecular ciliary process distance. Unlike traditional UBM, ASOCT can scan angle to angle at once and use this advantage to develop some new anatomic parameters such as anterior chamber width (ACW) and lens vault (LV) to detect angle-closure related disease.

Acquired ASOCT images are further analyzed with software. Using the built-in software on the Visante OCT, once you identify the scleral spur, it can automatically measure TISA500, TISA750, AOD500, and AOD750. Using the caliper function, the Visante OCT can also manually obtain information about ACW, LV, and iris thickness. In addition to the built-in software on the Visante OCT, the ImageJ (Image processing and analysis in Java; National Institutes of Health, Bethesda, MD) and the Zongshan Angle Assessment Program (ZAAP, Guangzhou, China) are other commonly used image processing software for ASOCT studies. While using the ZAAP, operators only need to identify the scleral spurs, and then the software can automatically calculate the ASOCT parameters. These image processing software programs have helped move the screening for angle-closure disease into a new era.

2.1. Anterior chamber angle

It would seem straightforward to determine the anterior chamber angle status by measuring the number of degrees of the angle. One of the problems with this software is the difficulty in placement of the apex and edge points of the "angle" that the observer drags and alters on the computer to define angle parameters. Pavlin and colleagues[12] proposed that the superior line be drawn through the trabecular meshwork (i.e., 250 μm from the sclera spur) and the inferior one along the anterior iris surface. However, defining the angle in degrees is somewhat subjective due to variations in iris configuration. Since the determination of the angle apex and angle sides is quite examiner-dependent, the reproducibility of anterior chamber angle measurements for repeated measurements in angle-closure screening is questionable.[12]

2.2. Angle opening distance

The AOD (Fig. 1) is the distance between the cornea and iris along a line perpendicular to the cornea at a specified distance (in μm) from the scleral spur.[12]

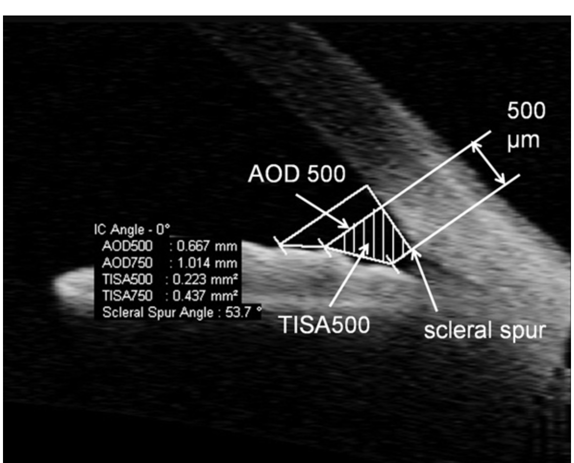

Fig. 1. Measurement of quantitative parameters using anterior segment optical coherence tomography (ASOCT). Illustrated are angle opening distance (AOD) and trabecular-iris space area (TISA).

2.3. Angle recess area

The ARA is the area lying between the line taken for the AOD and the angle recess.[13]

2.4. Trabecular iris space area

The TISA (Fig. 1) excludes the nonfunctioning area posterior to the scleral spur. The defining boundaries for the trapezoidal area are as follows: anteriorly, the AOD; posteriorly, a line drawn from the scleral spur perpendicular to the plane of the inner scleral wall to the opposing iris; superiorly, the inner corneoscleral wall; inferiorly, the iris surface.[14]

2.5. Trabeculo-iris contact length

Radhakrishnan and colleagues[14] proposed this parameter to describe an anatomically closed angle. The trabeculo-iris contact length is defined as the linear distance of iris contact with the corneoscleral surface, beginning at the scleral spur and extending anteriorly in an anatomically apposed or synechially closed angle.[14]

2.6. Iris thickness, curvature, area, and volume

Similar to the definition used in UBM examination, iris thickness in ASOCT images can be assessed using the scleral spur as a reference point to measure iris thickness at a certain distance from the scleral spur.

To calculate iris curvature (IC) (Fig. 2), the software draws a line from the most peripheral to the most central points of iris pigment epithelium, and then a perpendicular line is extended from this line to the iris pigment epithelium at the point of greatest convexity.[15]

The iris cross-sectional area is defined as the cumulative cross-sectional area of the full length of the iris from the scleral spur to the pupil margin.[16]

On the basis of the Pappus–Guldin centroid theorem, one can use iris cross-sectional area to estimate iris volume.[17]

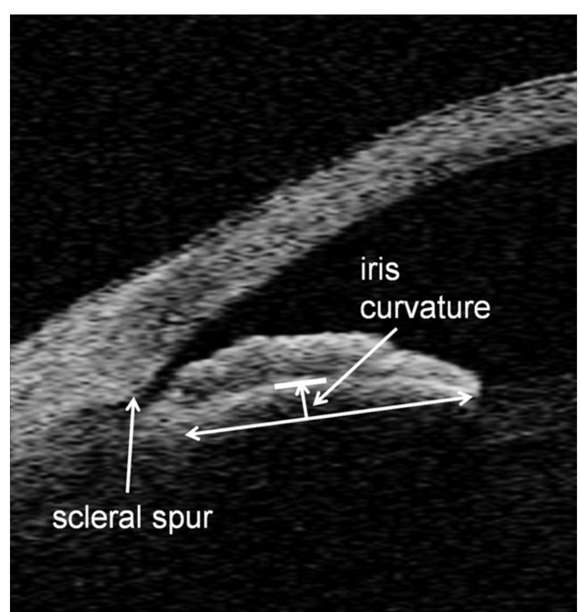

Fig. 2. Iris curvature measurement by ASOCT.

2.7. Lens vault

Nongpiur and colleagues[18] thought that the extent of the lens located anterior to the plane of the angles may play a role in the pathogenesis of angle closure. They developed a new parameter, LV (Fig. 3), defined as the perpendicular distance between the anterior pole of the crystalline lens and a horizontal line joining the two scleral spurs.[18]

2.8. Anterior chamber width, area, and volume

ACW (Fig. 3) is defined as the horizontal scleral spur-to-scleral spur distance.[19] Anterior chamber area (ACA) is the area whose boundaries are the corneo–scleral inner surface and the anterior iris and lens surfaces. Anterior chamber volume (ACV) is based on the ACA and is estimated by mathematical calculation.[20]

3. Differences in ASOCT parameters between open-angle and angle-closure eyes

Logically, eyes with narrow angles should have smaller anterior chamber angle, shorter AOD, smaller ARA, smaller TISA, and longer trabeculo-iris contact length. The AOD is somewhat influenced by the variability in the anterior iris surface since a relatively high point along the iris will yield a smaller AOD, and a relatively lower point will yield a larger AOD. ARA and TISA, which are bounded by AOD, are also influenced by the variability in iris configuration.

The iris may play an important role in the pathogenesis of angle closure. In a large community-based population study in Singapore, Wang and colleagues[16] reported that greater IC, area, and thickness were independently associated with narrow angle. Dynamic change in iris parameters before and after pupil dilation is another important issue for the pathogenesis of angle-closure disease. It is not surprising that iris thickness will be increased after pupil dilation either due to dim condition or mydriatics.[17] Although iris thickness is increased after pupil dilation, Quigley and colleagues[21] found that iris area is decreased after pupil dilation in both eyes with open angles and narrow angles. Aptel and Denis[17] also found that iris area was decreased after pupil dilation with mydriatics. The change is more prominent in eyes with open angles. However, the estimated iris volume was increased in eyes with narrow angles, but decreased in eyes with open angles.[17] Quigley and colleagues[21] think that the visible holes and crypts on the anterior iris surface permit aqueous passage through both macroscopic and microscopic channels into and out of the iris. If aqueous is able to move from the anterior chamber through the iris stroma, eyes with extensive iris-meshwork apposition may still maintain normal intraocular pressure.[21]

LV is another important ASOCT parameters related to angle closure. Nongpiur and colleagues reported that eyes with angle closure not only have thicker lenses but also greater LV compared to normal eyes (901 ± 265 vs. 316 ± 272 μm; $p < 0.001$). This parameter is independently associated with angle closure after adjusting for age, gender, ACD, and LT.[18] Another large-scale prospective cross-sectional study in Singapore, which included 1465 individuals for analysis, also showed that eyes with narrow angles had greater LV compared to eyes with open angles (775.6 vs. 386.5 μm; $p < 0.0001$). Women had significantly greater LV than men (497.28 vs. 438.56 μm; $p < 0.001$), and LV increased significantly with age (p for trend <0.001). Adjusted for age and sex, significant associations with greater LV were shorter AL, shallower ACD, higher intraocular pressure, and more hyperopic spherical equivalent (all $p < 0.001$). Tan et al[22] conclude that LV was independently associated with narrow angles and may be useful in screening to detect eyes with narrow angles. Ozaki et al[23] reported that increased LV was significantly associated with angle-closure [odds ratio (OR) 24.2; 95% confidence interval (CI), 2.3–250.5, comparing lowest and highest quartiles]. Although the OR associated with angle closure was 2.59 for LT, the 95% CI ranged from 0.48 to 13.85, which suggests that there is a wide variation in the association between LT and angle closure.[23]

ACW, ACA, and ACV are other anatomic parameters which can be measured by ASOCT but not by UBM. Nongpiur et al[18] screened 1465 community-based individuals and found that ACW was significantly smaller in women compared with men (11.70 vs. 11.81 mm, respectively; $p < 0.001$) and decreased significantly with age (p for trend <0.001). Participants with lower educational level, lower body mass index, shorter AL, shallower ACD, and Chinese race tended to have smaller ACW. Of the 1465 participants, 315 (21.5%) had narrow angles on gonioscopy. Mean ACW was smaller in eyes with narrow angles compared with those without narrow angles (11.60 vs. 11.80 mm; $p < 0.001$). Hospital-based participants with PAC/PACG had even smaller ACW than community participants with narrow angles (11.33 vs. 11.60 mm; $p < 0.001$). These findings implicate a smaller ACW as a risk factor for angle closure.[19] In a clinic-based study, Wang et al[24] reported that ethnic Chinese had smaller ACA/ACV independent of ACD, ACW, IC, iris area, pupil diameter, corneal radius, and AL when compared with Caucasians.

ASOCT also has been utilized in the evaluation of the anterior chamber before and after laser iridotomy. In a small case series, which enrolled 17 patients undergoing iridotomy, it was shown that the AOD500 and TISA750 were increased after laser iridotomy.[25] Recently, another larger-scale study, which enrolled 176 individuals with primary angle-closure suspicion, evaluated the change in anterior segment morphology after laser iridotomy.[26] A significant increase in the angle width was noted in participants with PACS after laser iridotomy. ACA and ACV increased after laser iridotomy, but there was no change in ACD, ACW, LV, IT, or IA; the increase in ACA/ACV was mainly due to decreased IC after laser iridotomy.

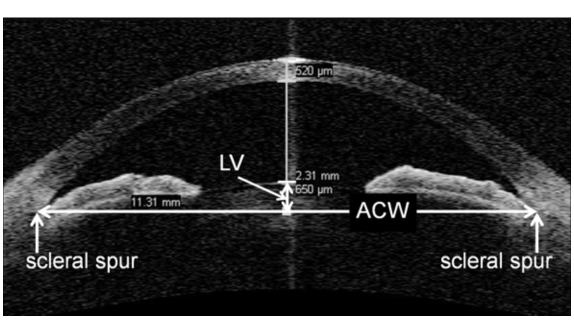

Fig. 3. Measurement of quantitative parameters using ASOCT. Illustrated are lens vault (LV) and anterior chamber width (ACW).

4. Limitations of ASOCT

It is a necessary step to identify the scleral spur first for most quantitative measurements about anterior chamber structures. However, the scleral spur is not always clearly identifiable in the ASOCT images. The scleral spur could not be clearly identified in 22.8% of angles in a community-based ASOCT imaging study.[19]

Although ASOCT can acquire high-resolution anterior chamber images for objective and quantitative evaluation, the images are limited to the cross sections of the anterior chamber that is imaged, and the remainder of the angle circumference is not assessed. The swept source OCT is a novel anterior segment imaging device that uses a swept laser source at a wavelength of 1310 nm and a scan speed of 30,000 A-scan per second.[27] It can acquire threedimensional anterior chamber images and create "gonioscopic views" to mimic the clinical gonioscopic effects.

Due to the influence of eyelids, ASOCT is less likely to obtain a good image at the superior and inferior angles. Such restriction may impede the accuracy of the measurement of IV and ACV.

When we use gonioscopy to evaluate angle, we can differentiate synechial closure from appositional closure by applying pressure on the gonioscopy lens. However, we cannot differentiate these two situations by ASOCT.

Although many ocular parameters are quite different between narrow-angle eyes and open-angle eyes, these may not be the most important determining factors for development of an acute primary angle-closure attack.

5. Conclusion

Wide scanning area with good image resolution and good reproducibility in repeated measurements make ASOCT popular for anterior segment imaging studies of angle-closure disease. Both static and dynamic measurements of ASOCT parameters are helpful to realize the pathogenesis of angle closure disease.

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