Special Focus, Glaucoma, Original Article

Comparison of anterior chamber angle parameters and iris structure of juvenile open-angle glaucoma and pigmentary glaucoma

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Purpose: To compare the quantitative measurements of the anterior chamber angle (ACA) and iris parameters in patients with juvenile open-angle glaucoma (JOAG), pigmentary glaucoma (PG), and healthy controls using anterior segment optical coherence tomography (AS-OCT). **Methods:** This was a retrospective, cross-sectional study of 25 eyes with JOAG, 25 eyes with PG, and 25 control eyes. Anterior chamber depth, angle-opening distance 500 and 750, trabecular–iris space 500 and 750, scleral spur angle, iris thickness (IT, measured at the thickest part), and iris bowing were obtained using AS-OCT (Visante" OCT 3.0 Model 1000, Carl Zeiss Meditec, Inc). **Results:** The quantitative ACA parameters were found to be significantly higher in JOAG and PG patients compared to healthy controls ($P < 0.001$); there was no significant difference between the eyes with JOAG and PG ($P > 0.05$). In eyes with JOAG and PG, there was significantly backward bowing of the iris in temporal and nasal angles compared to control subjects ($P < 0.001$). Median iris bowing was not significantly different between the patients with JOAG and PG ($P > 0.05$). The temporal and nasal angle iris thickness were significantly thinner in eyes with JOAG than the eyes with PG ($P < 0.001$) and age-matched control subjects ($P < 0.001$). The median IT did not differ between the patients with PG and control subjects ($P > 0.05$). In patients with JOAG, the intraocular pressure (IOP) was inversely correlated with IT ($r = -0.43$, $P < 0.05$). **Conclusion:** AS-OCT provided quantitative data on the ACA and iris parameters in JOAG and PG. The evaluation of the ACA and iris structures using AS-OCT revealed higher ACA measurements and posterior bowing of the iris in patients with JOAG and PG. Furthermore, the patients with JOAG were found to have thinner IT than the ones with PG and healthy controls.

Key words: Anterior chamber angle, anterior-segment optical-coherence tomography, ıris thickness, juvenile open-angle glaucoma, pigmentary glaucoma

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Juvenile open-angle glaucoma (JOAG) is an aggressive subtype of primary open-angle glaucoma (POAG) with an age of onset of 3–40 years and typically autosomal dominant inheritance.[1-3] It has similar characteristics as adult-onset POAG. However, JOAG is associated with more severe visual field loss, higher intraocular pressure (IOP) levels, and fluctuations. JOAG has been associated with the male gender and myopia.[2] Many individuals are asymptomatic until the field loss is advanced.[4]

Pigmentary glaucoma (PG) is secondary open-angle glaucoma characterized by the dispersion of pigment granules from the iris and its accumulation throughout the anterior segment, including the trabecular meshwork. Pigment accumulation in the trabecular meshwork reduces aqueous humor outflow and causes visual field damage with an increase in IOP.[5] PG occurs mostly in the third to fourth decades of life and has a male predominance, with the typical patient being a young man with moderate–severe myopia.[6]

Diagnosis of JOAG and PG is performed with a thorough clinical evaluation involving gonioscopy. Gonioscopy reveals a wide-open anterior chamber angle (ACA) in patients with JOAG. However, dysgenesis of the angle may be present with severe elevation of IOP.[7] The classic gonioscopic view in PG is a wide, open-angle with heavy, homogeneous trabecular meshwork pigmentation.[8]

Gonioscopy is the gold standard clinical technique that is used to examine ACA and iris, and enables evaluation and diagnosis of glaucoma subtypes. It is observer-dependent and is subject to intrinsic intra- and inter-individual variability. Anterior-segment optical-coherence tomography (AS-OCT) has emerged as an objective and noncontact complementary tool that provides high image resolution for visualization of the ACA and iris structures.[9,10] Visante AS-OCT (Carl Zeiss, Meditec, Dublin, CA, USA) is a machine that can be used for visualization and quantitative measurements of iris, iridocorneal boundaries, and the angle configurations.[11-14]

We speculate that patients in the JOAG group and in the PG group, who may be in the same age group and have similar risk factors such as male gender and myopia, may differ from each

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other in terms of ACA and iris structure. The purpose of the present study was to compare the quantitative measurements of ACA and iris parameters among the patients with JOAG, the patients with PG, and healthy subjects using AS-OCT.

Methods

This retrospective, cross-sectional study included patients with JOAG, patients with PG, and healthy subjects. The study included newly diagnosed patients who underwent AS-OCT between December 2018 and December 2020 as part of a work-up for glaucoma diagnosis. Patients were enrolled from the glaucoma division of a tertiary eye hospital. Healthy controls were recruited among age-matched hospital employees who had no clinical signs of glaucoma. The study was conducted following the Declaration of Helsinki principles, and the local medical ethics committee approved the research.

The criteria which were used for JOAG diagnosis were an age range from 18 to 40 years with an elevated IOP ≥ 21 mmHg by Goldmann applanation tonometry at the initial hospital visit, open-angle configuration on gonioscopy, glaucomatous optic neuropathy with neural rim thinning, focal notching or a vertical cup-to-disc ratio > 0.6 and/or glaucomatous visual field defects, and absence of history or signs of congenital glaucoma (i.e., buphthalmos, Haab's striae). PG was diagnosed with the presence of Krukenberg spindles, elevated IOP ≥21 mm Hg, presence of hyperpigmented trabecular meshwork, and glaucomatous optic neuropathy accompanied by visual field loss.

Patients who had undergone medical, laser, or surgical IOP-lowering treatment, history of ocular surgery, history of trauma, any other anterior segment abnormalities (e.g., corneal opacity or intumescent cataract), and those with other causes of secondary glaucoma in the same age range were excluded from the study.

All patients underwent comprehensive ocular examination including best-corrected visual acuity (BCVA) using Snellen charts, slit-lamp biomicroscopy, IOP measurement with Goldmann applanation tonometry, gonioscopy using a three-mirror lens, and dilated fundoscopy with a 90 D lens. Ultrasonographic pachimetry (DGH-550, DGH Technology Inc., Exton, PA, USA) was used to measure the central corneal thickness (CCT). Peripapillary retinal nerve fiber layer (pRNFL) thickness measurement by spectral-domain optical coherence tomography (SD-OCT) (OCT Spectralis, Heidelberg Engineering, Heidelberg, Germany) and visual field testing by Humphrey standard automated perimetry (HFA; Carl Zeiss Meditec, Dublin, CA, USA) were performed.

The quantitative ACA and iris parameters were measured using AS-OCT (Visante" OCT 3.0 Model 1000, Carl Zeiss Meditec, Inc) in the sitting position by a single masked examiner (BB) in room illuminating conditions. The examiner manually assigned the location of the scleral spur, and the following parameters for each image were automatically obtained from the Anterior Segment Analysis Program following the methods of previously published study.[15]

We recorded anterior chamber depth (ACD, mm; anteroposterior distance from the corneal epithelium to the lens surface), angle-opening distance 500 and 750 (AOD-500 and AOD-750, mm; distance from the cornea to iris at 500 μm or 750 μm from the scleral spur), trabecular–iris space 500 and 750 (TISA-500 and TISA-750, mm^2; area of the trapezoid between the iris and cornea from the scleral spur to 500 μm or 750 μm), scleral spur angle (SSA; the angle measured at the conjunction of the line connecting the scleral spur to the AOD-500 iris endpoint and the line connecting the scleral spur to the AOD-500 corneal endpoint), iris thickness (IT, mm; measured at the thickest part), and iris bowing (IB, mm; the maximum distance from the posterior surface of the iris to the line from posterior iris at the pupillary margin to the iris root).

The Shapiro-Wilk test was used to determine whether the data had a normal distribution. For assessments of ACD, temporal and nasal angles quantitative ACA (AOD-500, AOD-750, TISA-500, TISA-750, SSA), and iris parameters (IT, IB) were used. The eyes with higher initial IO*P* values before anti-glaucoma treatment were used in the analysis. One-way ANOVA and Kruskal Wallis tests were used to assess comparisons among three groups. Pairwise comparisons of the quantitative differences of ACA and iris parameters in patients with JOAG, PG, and healthy controls were analyzed with the Mann–Whitney U test. Spearman's Correlation Analysis was used to determine the correlation between IOP and iris thickness. In parametric tests, mean and standard deviation, in nonparametric tests, the median (1^{st} quarter–3^{rd} quarter) was used in the analysis. The Chi-square test was used to compare categorical data. $P < 0.05$ was considered statistically significant.

Results

The study included 25 eyes of 25 patients with JOAG, 25 eyes of 25 patients with PG, and 25 eyes of 25 healthy subjects. The demographic and ophthalmic characteristics of the three groups are summarized in Table 1. The patients with JOAG and PG were similar concerning age, gender, race, BCVA, IOP, C/D ratio, pRNFL, and mean deviation (Mann–Whitney U test, $p > 0.05$).

Median CCT was 550 μm (range, 530–575 μm) in the JOAG group, 535 μm (range, 525–547 μm) in the PG group, and 545 μm (range, 537.5–550 μm) in the healthy subjects. The median ACD was 3.51 mm (3.22–3.81 mm) in JOAG, 3.27 mm (2.99–3.66 mm) in PG, and 3.57 mm (3.33–3.73 mm) in the control group. The CCT and ACD parameters were statistically insignificant among the three groups (Kruskal Wallis test, $p > 0.05$).

Dense pigmentation of trabecular meshwork with wide-open ACA was found in eyes with PG, and dysgenesis of the angle and high iris insertion were present in eyes with JOAG on gonioscopy.

The temporal and nasal angle quantitative ACA parameters (AOD-500, AOD-750, TISA-500, TISA-750, SSA) in eyes with JOAG, PG, and the healthy controls are displayed in Table 2. All ACA parameters detected by AS-OCT were found to be significantly higher in patients with JOAG and PG compared to healthy controls ($P < 0.001$), but there were no statistically significant differences in any ACA parameters between the eyes with JOAG and PG ($P > 0.05$) [Fig. 1].

Fig. 2 presents the quantitative measurements of ACA parameters. The mid-peripheral iris configuration in eyes with JOAG was found to be significantly concave in 16

Table 1: Summary of Demographics and Ophthalmic Characteristics of Juvenile Open-Angle Glaucoma Patients, Pigmentary Glaucoma Patients, and Healthy Controls

	Patient groups			
	JOAG (*n*=25)	PG (*n*=25)	Control group (*n*=25)	*P*†
Age (years)	28.12±4.76	30.08±3.93	29.24±3.54	0.342
Gender (F/M)	6/19	7/18	10/15	0.581
Race, no. (%)				
Caucasian	25 (100%)	25 (100%)	25 (100%)	0.912
BCVA LogMAR	0 (0;0.2)	0 (0;0.15)	0 (0-0)	0.08
IOP (mmHg)	30 (26;34.5)	26 (22.5;31)	15 (12.5-16)	<0.001*
C/D ratio	0.7 (0.7;0.8)	0.7 (0.7;0.8)	0.3 (0.2-0.40)	<0.001*
pRNFL	78.84±19.87	87.53±7.51	114.44±4.71	<0.001*
MD (dB)	-7.52 (-8.50;-5.52)	-5.97 (-7.25;-4.54)	-0.85 (-1.275;-0.445)	<0.001*

For normally distributed variables, results are shown in mean±standard deviation; otherwise in median (1st quarter; 3rd quarter); †One-way ANOVA, Kruskal Wallis test; *Significant JOAG vs Control and PG vs control. JOAG=Juvenile open-angle glaucoma; PG=Pigmentary glaucoma; F=Female; M=Male; BCVA=Best corrected visual acuity; IOP=Intraocular pressure; pRNFL=Peripapillary retinal nerve fiber layer thickness; MD=Mean deviation

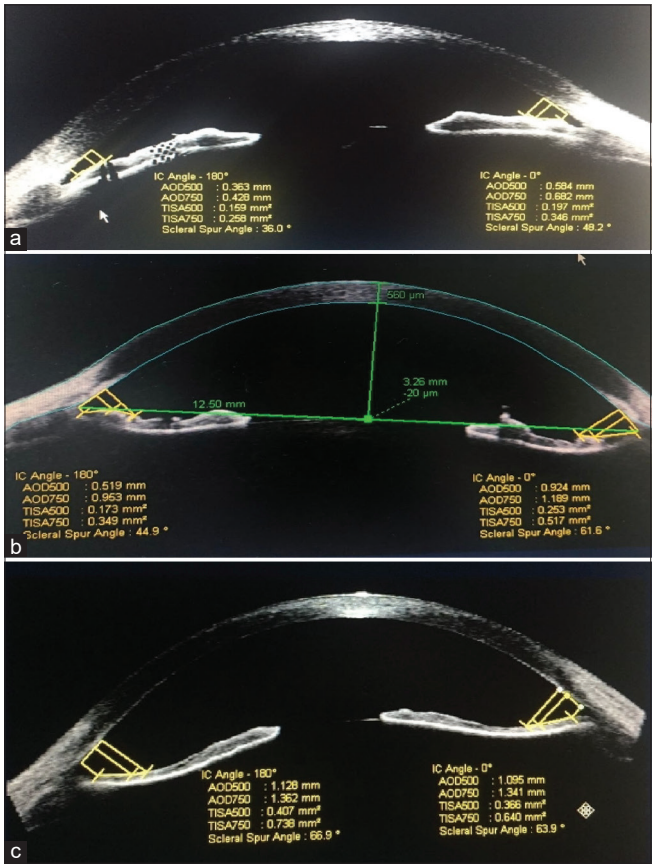

Figure 1: Visante AS-OCT scan (Carl Zeiss, Meditec, Dublin, CA, USA) demonstrating quantitative anterior chamber angle parameters of a healthy subject (a), patient with pigmentary glaucoma (b), and patient with juvenile open-angle glaucoma (c)

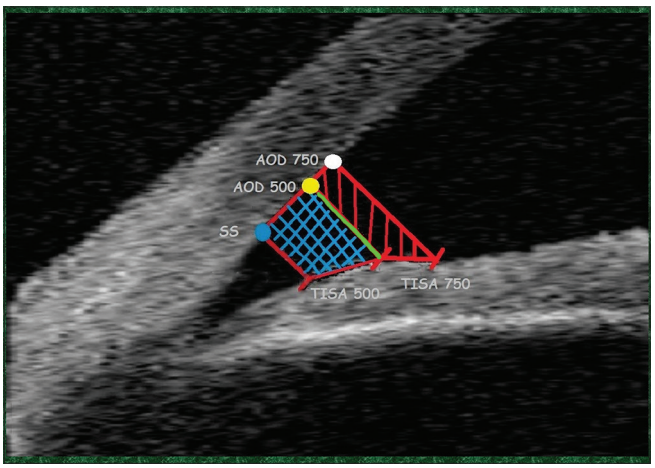

Figure 2: Diagram of the quantitative measurements of the anterior chamber angle parameters measured by Visante AS-OCT. The green line represents AOD 500, angle-opening distance (AOD) at 500 µm from the scleral spur (SS) and the red line represents AOD 750, the AOD at 750 µm from the SS. The grid sector represents TISA 500, the trabecular-iris space area (TISA) at 500 µm from the SS whereasTISA 750, the TISA at 750 µm from the SS, does that for grid plus striated sectors

eyes (64%) and planar in nine eyes (36%). In eyes with PG, the mid-peripheral iris configuration was concave in 25 eyes (100%), whereas in the control group the majority of the iris configuration was convex (72%). In eyes with JOAG and PG, there was significantly backward bowing of the iris in temporal and nasal angles compared to control subjects ($P < 0.001$). Median iris bowing was not significantly different between the patients with JOAG and PG ($P > 0.05$).

The temporal and nasal angle iris thicknesses were significantly thinner in eyes with JOAG when compared with the eyes with PG ($P < 0.001$) and age-matched control subjects ($P < 0.001$). The median IT did not differ between patients with PG and control subjects ($P > 0.05$). Table 3 summarizes the iris configuration, IB, and IT measurements for comparison among JOAG, PG, and healthy controls. Fig. 3 shows three representative cases (A–C) in which the IB and IT were measured to illustrate the study groups.

Correlation analysis in patients with JOAG demonstrated that the IOP was inversely correlated with the IT ($P = 0.03$) with a correlation coefficient r = -0.43 [Fig. 4].

Table 2: Comparison of Quantitative Anterior Chamber Angle Parameters In Eyes with Juvenile Open-Angle Glaucoma, Pigmentary Glaucoma, and Healthy Controls

	AOD-500 temporal	AOD-750 temporal	TISA-500 temporal	TISA-750 temporal	SSA temporal	AOD-500 nasal	AOD-750 nasal	TISA-500 nasal	TISA-750 nasal	SSA nasal
JOAG	1.30 (0.80-1.44)	1.61 (1.04-1.96)	0.41 (0.24-0.49)	0.81 (0.49-0.90)	69.60 (57.9-72.35)	1.09 (0.81-1.26)	1.31±0.48	0.34±0.18	0.62±0.28	59.42±14.23
Control group	0.40 (0.24-0.51)	0.59 (0.44-0.69)	0.15 (0.08-0.19)	0.25 (0.17-0.34)	39.1 (25.75-45.85)	0.45 (0.32-0.58)	0.65±0.30	0.14±0.08	0.28±0.15	38.93±15.09
P[a]	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
PG	1.11 (0.81-1.60)	1.49 (1.15-2.00)	0.39 (0.25-0.52)	0.73 (0.51-1.02)	67.4 (59.55-73.75)	1.08 (0.63-1.59)	1.39±0.49	0.40±0.19	0.71±0.30	62.32±10.57
Control group	0.40 (0.24-0.51)	0.59 (0.44-0.69)	0.15 (0.08-0.19)	0.25 (0.17-0.34)	39.1 (25.75-45.85)	0.45 (0.32-0.58)	0.65±0.30	0.14±0.08	0.28±0.15	38.93±15.09
P[a]	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
JOAG	1.30 (0.80-1.44)	1.61 (1.04-1.96)	0.41 (0.24-0.49)	0.81 (0.49-0.90)	69.60 (57.9-72.35)	1.09 (0.81-1.26)	1.31±0.48	0.34±0.18	0.62±0.28	59.42±14.23
PG	1.11 (0.81-1.60)	1.49 (1.15-2.00)	0.39 (0.25-0.52)	0.73 (0.51-1.02)	67.4 (59.55-73.75)	1.08 (0.63-1.59)	1.39±0.49	0.40±0.19	0.71±0.30	62.32±10.57
P[a]	0.581	0.541	0.342	0.332	0.563	0.491	0.563	0.254	0.301	0.423

For normally distributed variables, results are shown in mean±standard deviation; otherwise in median (1st quarter; 3rd quarter). JOAG=Juvenile open-angle glaucoma; PG=Pigmentary glaucoma; AOD-500=Angle-opening distance 500 (mm); AOD-750=Angle opening distance 750 (mm); TISA-500=Trabecular-iris space 500 (mm²); TISA-750=Trabecular-iris space 750 (mm²); SSA=Scleral spur angle. [a]Mann-Whitney U test; *Significant

Figure 3: (a) Left panel. Visante AS-OCT scan (Carl Zeiss, Meditec, Dublin, CA, USA) showing iris bowing measurement from a healthy subject. Right panel. Iris thickness measurement of the same eye. (b) Left panel. Visante AS-OCT scan showing iris bowing measurement from a patient with pigmentary glaucoma. Right panel. Iris thickness measurement of the same eye. (c) Left panel. Visante AS-OCT scan showing iris bowing measurement from a patient with juvenile open-angle glaucoma. Right panel. Iris thickness measurement of the same eye

Discussion

In the present study, using AS-OCT, we demonstrated that the quantitative ACA parameters differ in patients with JOAG and in patients with PG compared to healthy subjects. In patients with JOAG and in patients with PG, the ACA parameters were higher compared to healthy controls. The ACA parameters were not significantly different between the eyes with JOAG and the eyes with PG. Iris configuration was considerably concave, and the iris was significantly backward bowing in patients with JOAG and in patients with PG compared to control subjects. Remarkably, the IT was thinner in JOAG patients compared to PG patients and control subjects. However, in patients with PG, the IT was not significantly different than healthy controls.

The higher ACA parameters in eyes with JOAG and in eyes with PG demonstrate that the ACA is wider in these patients than in healthy subjects. In the literature, clinical studies reported significantly wider ACA with ultrasound biomicroscopy and deeper anterior chamber depth with optical biometry in the JOAG patients than in the normal subjects.[4,16] Likewise, using slit-lamp optical coherence tomography, increased anterior chamber depth and angle parameters were shown in patients with PG.[17] Although there is a general tendency to rely on AOD at 500 μm as the best estimate of angle opening,[17,18] in our study using AS-OCT, we additionally investigated TISA at 500 μm and 750 μm from the scleral spur, with quantitative assessment of iris bowing and iris thickness. The detailed evaluation of the ACA and iris parameters using AS-OCT revealed significantly increased ACA dimensions with posterior bowing of the iris in patients with JOAG and in patients with PG compared to the healthy controls.

The present study indicates significantly backward bowing and concave iris configuration (64%) in JOAG patients than healthy controls. In PG patients, all eyes had a backward bowing and concave configuration of the iris.

Table 3: Comparison of Quantitative Iris Parameters In Eyes with Juvenile Open-Angle Glaucoma, Pigmentary Glaucoma, and Healthy Subjects

	JOAG (*n*=25)	PG (*n*=25)	Control Group (*n*=25)	*P*		
				JOAG vs Controls	PG vs Controls	JOAG vs PG
Iris shape (concave/flat/convex)	16/9/0	25/0/0	3/4/18	<0.001*	<0.001*	0.002*
Iris bowing						
Temporal quadrant	-0.26 (-0.49; 0.11)	-0.29 (-0.41; -0.24)	0.12 (0-0.15)	<0.001*	<0.001*	0.501
Nasal quadrant	-0.28 (-0.42; 0.06)	-0.24 (-0.36; -0.18)	0.12 (0-0.16)	<0.001*	<0.001*	0.562
Iris thickness						
Temporal quadrant	0.28 (0.24; 0.31)	0.36 (0.31; 0.41)	0.48 (0.42-0.50)	<0.001*	0.062	<0.001*
Nasal quadrant	0.32 (0.25; 0.35)	0.40 (0.35; 0.41)	0.44 (0.41-0.49)	<0.001*	0.084	<0.001*

JOAG=Juvenile open-angle glaucoma; PG=Pigmentary glaucoma; *Significant

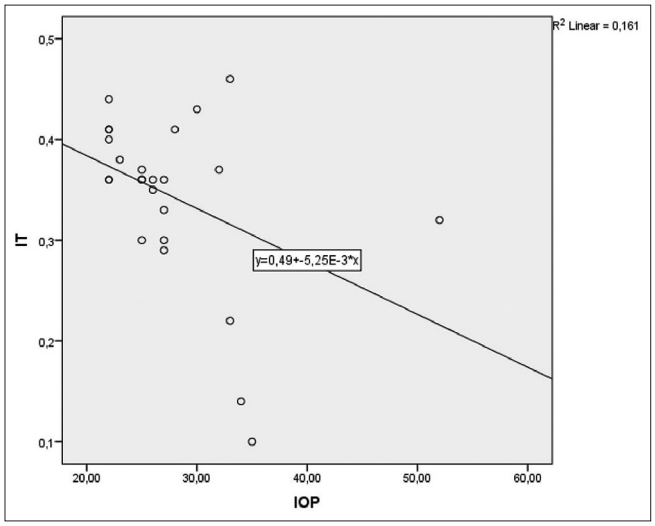

Figure 4: Scatterplot showing the correlation between the iris thickness (IT) and intraocular pressure (IOP) in patients with juvenile open-angle glaucoma ($P < 0.05$; correlation coefficient -0.43)

Although our findings are consistent with previous clinical studies demonstrating the backward bowing and concave iris configuration in PG,[17] to date, this is the first study to report backward bowing and mostly concave iris configuration in patients with JOAG compared to age-matched control subjects. As in ACA parameters, the difference in backward bowing of the iris in patients with JOAG and in patients with PG was not significant.

In the current study, we quantitatively demonstrated the IT to be thinner in patients with JOAG than in patients with PG and in control subjects. In PG, IT was not significantly different from healthy controls. In a recent study, the anterior segment of primary congenital glaucoma patients was evaluated using hand-held OCT, and a thinner iris attributed to reduced stromal thickness was found in 59.52%.[19] Our findings are in accordance with previous reports,[20] using AS-OCT, we detected concave and thinner iris in JOAG patients with a significant negative correlation between iris thickness and IOP. Therefore, we hypothesized that the thinner iris in patients with JOAG indicates the reduced stromal thickness in these patients, which might be due to stretching of the eye related to severely elevated and fluctuating IOP (1). Significant backward bowing of the iris compared to healthy controls also support this result. Iris structures may be more susceptible to damage due to elevated IOP in JOAG patients. Although Pilat *et al*. found no correlation between elevated IOP and iris thinning, unlike our study, they investigated younger primary congenital glaucoma patients.[19] The fact that our patients were in the juvenile age group and the presence of dysgenetic angle structures in gonioscopy made us think that they might have greater severity of damage and been exposed to high IOP for a longer period of time.

JOAG and PG are clinical pathologies that can resemble each other, especially in the early stages of the disease with IOP fluctuations when characteristic clinical findings are not evident. To date, there is no study comparing the quantitative evaluation of ACA and iris structures of patients with JOAG and PG using AS-OCT. A wide-open angle with increased ACA parameters and backward bowing of the iris was seen in both JOAG and PG patients. Significantly, in patients with JOAG, the IT tended to be thinner compared to PG. Documentation of peripheral iris contour and thickness measurement can provide critical additional information in diagnosing these two glaucoma subtypes, which can be seen in the same age group and may have common risk factors.

The Visante AS-OCT provides good-quality images for quantitative measurement of the ACA and iris structures with good reproducibility.[12] In clinical practice, AS-OCT is a substitute for gonioscopy when gonioscopy is not feasible due to corneal pathology or lack of patient cooperation. It has the advantage of being an objective and non-invasive method, comfortable, rapid, repeatable, and can be performed under dark conditions allowing angle assessment during physiological mydriasis.[17,21]

The strength of our study includes the enrolment of newly diagnosed patients with two different glaucoma subtypes in the same age groups before anti-glaucoma treatment.

Unlike gonioscopy, static assessment of the angle anatomy and technical limitations are major drawbacks of the study. Another limitation is the absence of refractive status of the control and the study groups. As this was the first study using AS-OCT to address visualization and comparison of the quantitative measurements of the ACA and iris structures in the JOAG patients, PG patients, and healthy controls, it was not comparable with similar publications. As the primary

finding of the study is decreased iris thickness among JOAG as compared to PG and normal controls among Caucasians, who have a thinner iris as compared to African and Asian people, whether the same findings are present in JOAG patients of other ethnicities will require further studies. Although the increasing number of AS-OCT parameters help better understand the ACA and iris anatomy and its relationship to glaucoma subtypes, this may cause some confusion in evaluating AS-OCT scans. With the advent of more sophisticated technology in the future, AS-OCT can provide more precise and detailed information on identifying iridocorneal angle structures and detecting associated anomalies.

Conclusion

Eyes with JOAG and eyes with PG showed higher ACA parameters and backward bowing of the iris when compared to control eyes. In patients with JOAG, the IT was thinner compared to patients with PG and healthy controls. In patients with JOAG, the IOP was inversely correlated to IT. Further prospective studies with a larger number of subjects and the normal value of ACA parameters and iris thickness, which is known to be varying in the general population are needed to assess the utility of these parameters as a diagnostic tool.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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