Anterior Segment Biometry in Primary Angle Closure Glaucoma Patients with Visual Field Progression: Comparison between Malays and Chinese

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ABSTRACT

Objective: To compare anterior segment biometry parameters in progress and non-progress primary angle closure glaucoma (PACG) among Malay and Chinese patients.

Materials and methods: A cross-sectional study was conducted between November 2015 and December 2016 involving 75 patients with PACG (43 Malays and 32 Chinese) who were recruited from a single glaucoma center in Malaysia. Ocular examination included anterior segment biometry measurements on the selected eye. Axial length (AL) and anterior chamber depth (ACD) measurement was done using a noncontact partial coherence interferometer (IOL Master, Carl Zeiss, Germany). Anterior chamber angle (ACA) was measured by Anterior Segment-OCT (Spectralis Heidelberg, Germany). Humphrey visual field (HVF) 24-2 analysis of the same eye was conducted and compared with the HVF when diagnosis was made. Progression of PACG patients was assessed according to the Hodapp, Parrish and Anderson's (HPA) classification, they were then divided into progress and non-progress groups. Comparison of anterior segment biometry parameters between Malay and Chinese PACG patients with and without progression was analyzed using independent T test. Multivariate ANOVA analysis was used to compare the anterior segment parameters between progress and non-progress PACG patients, with adjustment for age, gender, lens status, family history and presence of diabetes mellitus.

Results: Chinese PACG patients have significant shorter AL (22.18 mm ± 0.76) and narrower ACA (11.96° ± 6.00) compared to Malay PACG patients. Among the progress group, Chinese PACG patients have significant shorter AL, shallower ACD and narrower ACA compared to Malays. However, after controlling for confounding factors, there was significant difference in ACA between Malay and Chinese PACG. There was also no significant difference of ocular biometry measurement between Chinese and Malay patients in progress and non-progress group.

Conclusion: There was racial influence in ocular biometry measurement in PACG patients. Chinese have significant narrower ACA compared to Malays. Serial AS-OCT monitoring is important in management of PACG.

Keywords: Angle-closure glaucoma, Angle measurement, Anterior chamber angle.

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INTRODUCTION

Primary angle closure glaucoma (PACG) is characterized as a chronic, progressive visual field (VF) loss and optic nerve cupping, often associated with an elevated intraocular pressure (IOP) due to the presence of the iridotrabecular contact (ITC) by gonioscopy, which can either be appositional or synechial, in the absence of underlying secondary ocular disease.[1] Ethnic or geographic differences in the prevalence rates of PACG are well known, with relatively high prevalence rates of 1.1–2.0% in Chinese,[2,3] Mongol 1.4%,[4] Thai 0.9%,[5] Nepal 0.39%[6] and Singaporean Chinese 1.1%.[7]

The prevalence of PACG in Malays was 0.12% based on the Singapore Malay Eye Study that involved 3,280 participants aged 40–80 years.[8] There is minimal knowledge regarding the presentation of PACG in Malays. The majority of the studies were retrospective in nature.[9,10] The progression rate of PACG was higher in Malays in Malaysia compared to Chinese in Malaysia, Taiwan, and Hong Kong.[10] This observation was made on a small number of Malays in Malaysia. In another retrospective study, Malays demonstrated a 16-fold (95% confidence interval, $p = 0.001$) increased risk of progression in the presence of a glaucomatous optic disc.[11] In comparison with

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Chinese patients treated in another tertiary center in Malaysia, Malays were found to present with advanced disease, older age, higher baseline IOP, and progressed faster than Chinese.[11] In a retrospective observational case series based on the Chinese population in Singapore, a third of eyes with PACG experienced VF deterioration over 10 years, with 7% progressing to blindness while on treatment. Eyes with higher mean overall IOP and a

history of previous acute angle closure were more likely to have VF progression.[12]

Late presentation and poor awareness may contribute to the higher rate of progression among Malays. However, there is the possibility that racial differences play a role in the course of the disease.[13,2] Perhaps, genetics play a role in the determination of progression and ocular biometry.[14] Ocular biometry has been identified as a nonmodifiable risk factor for PACG.[15–19] Anterior segment biometry, shorter AL, shallow ACD, and small ACA have been identified to increase the risk of PACG.[7,17,18,20,21] Perhaps, anterior segment biometry plays a role as the risk factor for progression.

A shallower anterior chamber increases the risk of the formation of peripheral anterior synechiae (PAS) that may lead to further IOP elevation and progression of PACG.[23,20,24] The aim of this study was to compare the anterior segment biometry parameters between progress and nonprogress PACG patients among Malay and Chinese. Factors affecting the progression of PACG in Malays and Chinese were also evaluated in this study.

MATERIALS AND METHODS

Patient Recruitment

A cross-sectional study was conducted between November 2015 and December 2016. A total of 75 PACG patients (43 Malays and 32 Chinese) were recruited from a tertiary center, Ophthalmology Clinic in Hospital Universiti Sains Malaysia (HUSM), Kota Bharu, Kelantan, Malaysia. This study received ethical approval from the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia (USM/JEPeM/15060236) and was conducted in accordance with the Declaration of Helsinki for human research.

The current classification of PACG is based on clinical observations in European populations and can be classified into three types; primary angle closure suspect (PACS), primary angle closure (PAC), and PACG. PACS is defined as an eye in which 180° or more appositional contact between the peripheral iris and posterior trabecular meshwork is considered possible with normal IOP, no PAS, and no evidence of glaucomatous optic neuropathy (GON). PAC is defined as an eye with 180° or more occludable drainage angle and features indication that trabecular obstruction by the peripheral iris has occurred, such as raised IOP of >21 mm Hg, PAS, iris whirling, "Glaucomflecken" lens opacities, or excessive pigment deposition on the trabecular surface in the absence of GON. The term PACG is used to indicate PAC eyes with GON ("European Glaucoma Society," 2014; Foster et al., 2002).[20]

A pedigree chart was drawn to ascertain the Malay and Chinese lineage, only those with three generations of Malay and Chinese lineage without any interracial marriages were recruited. PACG patients with a minimal four reliable and reproducible VFs, including the current VF (two VFs at the diagnosis and two VFs at current recruitment), were included. All PACG patients had laser peripheral iridotomy (LPI) done prior to the recruitment period. Patients were excluded if they had an incomplete pedigree chart, an unknown pedigree chart, any intraocular surgery other than cataract surgery that may affect the natural anatomy of anterior segment biometry or a history of panretinal photocoagulation laser therapy. Those with a cataract of nuclear opalescence >2, cortical >2, and posterior subcapsular >2 based on the Lens Opacities Classification System III[25] or severe

corneal diseases that precluded adequate view of the anterior segment were also excluded. Written consent was obtained from selected patients prior to the commencement of the study.

Comprehensive ocular examination, including slit-lamp examination, gonioscopic evaluation, and IOP measurement using a Goldmann applanation tonometer, was conducted to rule out secondary causes of glaucoma, including secondary angle closure. The posterior segment was also evaluated to identify non-GON or retinal diseases affecting the interpretation of VF. Refractive assessment was also conducted to exclude patients with high refractive error, spherical equivalent <−8 or >+4 diopter. If both eyes fulfill the selection criteria, only the right eye is selected. Medical records were also retrieved to obtain data on the duration and treatment of PACG, history of acute primary angle closure (APAC), and systemic comorbidities (e.g., diabetes mellitus, hypertension, dyslipidemia, and ischemic heart disease). A direct face-to-face interview was conducted to obtain information on the education level and family history of glaucoma.

Humphrey visual field (HVF) 24-2 analysis was conducted during the recruitment period, and another repeated HVF evaluation was conducted 1 month after the recruitment period. Reliable VF was based on fulfilling criteria of ≤33% fixation losses, ≤33% false-negative results, and ≤33% false-positive results. Another repeat HVF was conducted within 6 months of the recruitment period if the second HVF was not reliable or reproducible. Two reliable, reproducible consecutive HVFs within 6 months of the diagnosis of PACG were retrieved from the medical record. Progression is based on the HVF changes using the HPA classification. The primary investigator (NPF) and glaucoma specialist (LS) were responsible for analyzing the HVF. The definition of progression was based on the agreement of both investigators. Based on the HPA classification, PACG patients were divided into progress and nonprogress groups.

Ocular biometry measurement was conducted by a trained optometrist who was blinded from the HVF analysis. AL and ACD were measured using a noncontact partial coherence interferometer (IOL Master, Carl Zeiss, Germany). AS-OCT (Spectralis Heidelberg, Germany) was used to measure the and ACA without pupil dilation in standard illumination conditions. A minimum of five images were obtained. The best image was chosen based on the operator's (optometrist) best judgement. Any image with motion or artifacts was excluded. Measurement of of ACA from the identified scleral spur was conducted by another blinded investigator (AY). The analysis between the anterior segment parameters and progression of glaucoma (based on HPA) according to the races was conducted using the statistical package for social sciences for windows version 22.

Statistical Analysis

Descriptive statistics were analyzed using the Statistical Package for the Social Sciences for Windows Version 22. Descriptive statistics were performed to analyze the demographic data. An independent *t*-test was used to compare the anterior segment biometry parameters between Malay and Chinese patients with and without the progression of PACG. A *p*-value of <0.05 was deemed statistically significant. MANOVA analysis was used to compare the anterior segment parameters between progress and nonprogress PACG patients, with adjustment for age, gender, lens status, family history, and presence of diabetes mellitus.

RESULTS

Chinese patients with PACG were significantly older ($p = 0.035$) (Table 1). There was a significant predilection toward females among Chinese patients with PACG, with a ratio of 2.5:1 (Table 1). The duration of the disease was significantly longer among the Malays compared to the Chinese ($p = 0.032$) (Table 2). There was a higher number of Chinese patients (53.1 %) with a positive family history of PACG compared to Malays (20.9%) (Table 2). However, there was a significant difference in the presence of APAC between the two races (Table 2).

Chinese patients with PACG have a significantly shorter AL (22.18 mm ± 0.76) and narrower ACA (11.96° ± 6.00) compared to Malays (Table 3). However, after adjustment for age, gender, family history, presence of diabetes mellitus, and lens status, only ACA differed significantly between Chinese and Malays (Table 3). In the progress group, Chinese patients have a significantly shorter AL, shallower ACD, and smaller ACA compared to Malays (Table 4). However, after controlling for confounding factors, there was no significant difference (Table 4). There was no significant difference in anterior segment biometry between Malay and Chinese PACG patients in the nonprogress group (Table 5).

DISCUSSION

Hyperopia, short AL, shallow ACD, and increased lens thickness[22,26–28] have been identified as ocular biometric changes associated with the risk of PACG. Previous studies have found that the ocular biometry of PACG differs from normal subjects in the Chinese population.[29–31] However, there is no comparison of ocular biometry between different races in Asia.

Based on our study, there was a statistically significant difference between AL and ACA between Malays and Chinese. Chinese patients with PACG have a significantly shorter AL and smaller ACA. However, there was no difference in ACD between Chinese and Malay PACG patients. ACD has been reported as the strongest predictor for PACG.[28] As ACD is measured from corneal epithelium and lens, the lens plays an important role as a determinant.[31]

In the present study, we included pseudophakic and phakic patients. The majority of our recruited Chinese patients with PACG (81.2%) were pseudophakic, while 34.9% of Malay patients with PACG were phakic. Pseudophakia caused changes in the ocular biometry (Nonaka et al., 2006; Memarzadeh et al., 2007; Dawczynski et al., 2007; Kasai et al., 2015). A prospective comparative observational case series by Mermazader et al. showed that the morphology of anterior segment biometry changed after cataract surgery. This included flattening the convex iris configuration and widening ACD and ACA (Memarzadeh et al., 2007). Another study also demonstrated an increase in ACD and ACA after cataract surgery with intraocular lens implantation (Dawczynski et al., 2007). Apart from this, lens position might have greater influences on angle width than lens thickness (Mermazader et al., 2007).

In addition, a significantly higher number of Chinese patients with diabetes mellitus may lead to inaccuracy. Diabetes mellitus is known to cause swelling of the lens and cornea that may cause falsely shallower ACD.[32,33] Moreover, the duration of postcataract extraction surgery was not included in the present study. A recent randomized control trial demonstrated the lowering of IOP by lens extraction.[34] Clear lens extraction showed effective greater efficacy and was more cost-effective than LPI in lowering IOP in PACG patients.[34]

On the contrary, there was no significant difference in ACD between Chinese, Caucasians, and Blacks.[35,36] Based on a study conducted by Congdon et al., the radius of corneal curvature was significantly smaller among the Chinese compared to the other two groups.[36] The radius of corneal curvature represents a crowded anterior chamber and angle rather than shallow ACD. In addition, ACD measures the central chamber depth but not the peripheral. It is postulated that the pathogenesis of angle closure in the Chinese population is due to crowding of the peripheral anterior chamber, plateau iris configuration, or a combination of these with the presence of pupillary block, rather than pure pupillary block.[37]

After controlling for confounding factors, such as age, gender, family history, lens status, and the presence of diabetes mellitus, there was a significant difference in ACA between the Malay and Chinese patients with PACG. There were minimal studies that

Table 1: Demographic data of Malay and Chinese PACG patients

	PACG (N = 75)		
Variables	Malay (N = 43)	Chinese (N = 32)	p-value
Mean age in years	63.7 ± 9.4	68.6 ± 10.0	0.035^
Gender (n,%)			
Male	22 (51.2%)	9 (28.1%)	0.045#
Female	21 (48.8%)	23 (71.9%)	
Systemic disease (n,%)			
Diabetes mellitus	33 (76.7%)	12 (37.5%)	0.001#
Hypertension	31 (72.1%)	27 (84.4%)	0.209#
Hyperlipidemia	35 (81.4%)	25 (78.1%)	0.726#
Ischemic heart disease	16 (37.2%)	13 (40.6 %)	0.294#
Educational level (n,%)			
No formal education	9 (20.9%)	5 (15.6%)	0.346#
Primary	17 (39.5%)	19 (59.4%)	
Secondary	13 (30.2%)	7 (21.9%)	
Tertiary	4 (9.3%)	1 (3.1%)	

#Pearson Chi-squared test ($p < 0.05$ is significant); ^independent t-test ($p < 0.05$ is significant)

Table 2: Comparison of glaucoma-related history and clinical features in Malay and Chinese PACG patients

	PACG (N = 75)		
Variables	Malay (N = 43)	Chinese (N = 32)	p-value
Mean duration of PACG in years	6.90 ± 3.6	5.30 ± 2.7	0.032^
Family history of glaucoma (n,%)	9 (20.9%)	17 (53.1%)	0.004#
APAC	23 (53.5%)	13 (40.6%)	0.270#
Mean IOP (mm Hg)	17	15	0.064#
Lens status (n, %)			
Phakic	5 (34.9%)	6 (18.8%)	0.124 #

APAC, acute primary angle closure; ^independent t-test (p < 0.05 is significant); #Pearson Chi-squared test (p < 0.05 is significant)

Table 3: Comparison of anterior segment biometry parameters between Malay and Chinese PACG patients

	PACG (N = 75)			
Variables	Malay (N = 43)	Chinese (N = 32)	p-value^	p-value*
Anterior segment biometry parameters				
Mean ± standard deviation (SD)				
AL (mm)	22.62 ± 0.76	22.18 ± 0.87	0.022^	0.124*
ACD (mm)	2.78 ± 0.54	2.61 ± 0.53	0.183^	0.361*
ACA (°)	14.43 ± 6.62	11.58 ± 5.32	0.042^	0.041*

Independent t-test (p < 0.05 is significant); *MANOVA test (p < 0.05 is significant); model adjusted for age, gender, family history, lens status, and presence of diabetes mellitus

Table 4: Comparison of anterior segment biometry parameters in Malay and Chinese PACG patients with VF progression

	Progress PACG (N = 47)			
Variables	Malay (N = 27)	Chinese (N = 20)	p-value^	p-value*
Anterior segment biometry parameters				
Mean ± SD				
AL (mm)	22.47 ± 0.78	22.01 ± 0.77	0.047^	0.878*
ACD (mm)	2.70 ± 0.55	2.40 ± 0.30	0.020^	0.345*
ACA (°)	11.96 ± 6.00	9.18 ± 2.37	0.032^	0.478*

^Independent t-test (p < 0.05 is significant); *MANOVA test (p < 0.05 is significant); model adjusted for age, gender, lens status, family history, and presence of diabetes mellitus

Table 5: Comparison of anterior segment biometry parameters in nonprogress Malay and Chinese PACG patients

	Nonprogress PACG (N = 28)			
Variables	Malay (N = 16)	Chinese (N = 12)	p-value^	p-value*
Anterior segment biometry parameters				
Years ± SD				
AL (mm)	22.89 ± 0.66	22.45 ± 1.00	0.184^	0.504*
ACD (mm)	2.92 ± 0.50	2.96 ± 0.64	0.845^	0.660*
ACA (°)	19.04 ± 5.18	15.58 ± 6.44	0.135^	0.091*

^Independent t-test (p < 0.05 is significant); *MANOVA test (p < 0.05 is significant); model adjusted for age, gender, lens status, family history, and presence of diabetes mellitus

included ACA in their ocular biometry assessment.[38–40] Perhaps, this is due to the difference in the technique of biometry assessment, as AS-OCT is a new imaging tool. ACA may provide a better predictor for the development of ITC. There was a direct correlation between the degree of ITC and PAS formation.[41,42] This may be indirectly associated with the progression of PACG.

Based on our findings, Chinese patients who developed VF progression had relatively shorter AL, shallower ACD, and narrower ACA compared to Malays. However, after controlling for confounding factors, there was no significant difference in AL, ACD, and ACA between Malay and Chinese PACG patients with progression. Shorter AL was found as a predictor for the progression of VF defects in Chinese patients with PACG.[43] Shorter AL is associated with greater circadian and postural-related changes in habitual IOP.[44,45] Changes in IOP may impose a direct mechanical effect on the optic nerve head or indirectly cause impairment in the ocular perfusion pressure.[46,47] On the contrary, the mean IOP was higher in Malay patients compared to Chinese. There was no documentation of IOP control throughout

the entire duration of the disease. In the present study, we assumed that the IOP was well-controlled and achieved the target IOP. PACG patients are known to develop wide fluctuation of IOP, especially those with acute on chronic type of presentation.[48,49]

On the contrary, Chinese patients were significantly older compared to Malays. Increasing age was found to be associated with decreasing AL and ACD.[50–53] Moreover, there were a higher number of men who developed PACG among Malay patients. Men are known to have deeper ACD and wider ACA.[53–56] Women are more at risk of developing a progression of PACG,[12] partially due to the overcrowding of the anterior chamber.[57] The difference in ocular biometry between races is most likely related to a genetic predisposition to the development and progression of the disease.[14,58] The complexity of PACG, the intermingling of genetics, environment, and other potential causes make the understanding of the disease more interesting.

Understanding the effect of ocular biometry changes in the progression of chronic diseases like PACG is not possible with a cross-sectional study. Perhaps, a prospective study will be a more appropriate methodology. The recruitment should begin at the diagnosis, and AS-OCT should be conducted as routine with serial assessment throughout the follow-up period. Furthermore, the sample size was relatively small, especially after dividing into progress and nonprogress groups. This is partly due to the inability to obtain reliable and reproducible VF at the baseline. Low education level and learning curve may affect the accuracy of VF analysis. In view of the multifactorial components that can contribute to this blinding disease, small sample sizes in our study might be unable to represent the exact population. Moreover, using HPA classification to detect VF progression is not an ideal technique.[59] However, the current study may provide useful insight into understanding PACG in Malays.

Conclusion

Ocular biometry may get influenced by the racial differences in Asians with PACG. Chinese have a significantly narrower ACA compared to Malays. However, the influence of ocular biometry in the progression of PACG is still inconclusive. Serial AS-OCT monitoring is important in the management of PACG.

Disclosure

This article is a part of the author's (Dr Neoh Pei Fang) dissertation titled "Evaluation of anterior segment biometry parameters in progress and non-progress PACG among Malays and Chinese" archived in the "Universiti Sains Malaysia Institutional Repository" (http://eprints.usm.my/45317/1/Dr.%20Neoh%20Pei%20Fang-24%20pages.pdf).

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