ORIGINAL ARTICLE

Comparison of Contrast Sensitivity and Central Corneal Thickness in Primary Open Angle Glaucoma Suspects and Visually Normal Participants

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ABSTRACT

Introduction: Glaucoma causes a reduction of contrast sensitivity (CS) while thinner central corneal thickness is (CCT) associated with the risk of glaucoma. Thus, in glaucoma suspect patients, CS and CCT measurements may better evaluate and monitor the disease. The purpose of this study was to compare CS and CCT between a Primary Open Angle Glaucoma (POAG) suspect group and a normal group of similar age. **Methods:** CS was measured with the Pelli-Robson CS chart, while CCT was measured with a hand-held pachymeter. In total, 115 glaucoma suspects and 102 normal participants were included. **Results:** There was a significant effect of the clinical condition on CS [$F(1,209)=5.409$, $p=0.02$]. The effect of age on CS was also significant [$F(3,209)=20.419$, $p<0.001$]. The interaction between age and clinical condition was not statistically significant [$F(3,209)=0.815$, $p=0.49$]. CS of POAG suspects was significantly lower than that of the normal group for the younger age groups (40 to 59 years old) but not for the older age groups (50 to 80 years old). There was no significant effect of clinical condition on CCT [$F(3,209)=0.754$, $p=0.39$]. However, there was a significant effect of age on CCT [$F(3,209)=3.789$, $p=0.01$]. **Conclusion:** Contrast sensitivity measurement is potentially useful to be integrated with routine investigations for POAG suspect patients, especially those who are younger than 60 years old. Measurements of central corneal thickness alone may not be able to differentiate between POAG suspects and visually normal individuals.
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Keywords: Contrast Sensitivity, POAG Suspect, Central Corneal Thickness

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INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide. The estimated number of people with glaucoma aged 40 to 80 will increase from 76 million in 2020 to 111.8 million in 2040, disproportionally affecting people residing in Asia (1). In Asia, the number of people with glaucoma is estimated to increase by 16% to 59.5 million in 2020 and by 57.6% to 80.87 million in 2040 (2). Because blindness due to glaucoma is irreversible, early detection of the disease is crucial to reduce the burden of irreversible blindness. Indeed, glaucoma patients at the early stage of the disease, even with normal visual acuity (VA), are reported to have a poorer quality of life (3). Therefore, early identification and treatment of patients with glaucoma and those at high risk of developing vision loss could reduce an individual's loss of health-related quality of life as well as the personal and social-economic burdens (4).

Glaucoma suspects are a group of individuals with clinical findings and/or risk factors that would lead to an increased probability of developing primary open-angle glaucoma (POAG) (5). The diagnosis of POAG depends on the characteristic of structural changes to the optic nerve head (ONH) and retinal nerve fibre layer (RNFL) with corresponding visual field (VF) defect. Even though VF assessment with standard automated perimetry is the gold standard to detect abnormalities indicative of glaucoma, it is a highly subjective test and does not detect visual field defects until approximately 30% to 50% of retinal ganglion cell axons have been lost (6). At least six reliable VF examinations are required in the first two years to establish a good set of baseline data to determine the rate of progression for the diagnosis of glaucoma (7, 8). Evaluation of the ONH to identify the presence of thinning of the optic nerve neuroretinal

rim, peripapillary retinal nerve fibre layer and the inners layer of the macula is heavily incorporated with imaging technology; the OCT. Thus, the OCT complements clinical examination in monitoring structural and functional changes in glaucoma suspects (9, 10). The performance of the OCT in screening for patients at the severe stage of the disease will be different from the identification of subjects with early glaucomatous damage (11), and diagnostic performance may be more accurate in the moderate to advanced stages of glaucoma rather than at earlier stages (12).

Contrast sensitivity has been shown to decrease in patients with glaucoma (13-17). It also reduces at different stages of the disease (18). Although it is known that normal ageing also results in a reduction of contrast sensitivity, the presence of glaucoma causes a further decrease of sensitivity because of the impaired retinal ganglion cell in early glaucoma (19). The measurements of contrast sensitivity has been shown to facilitate an early detection of POAG (18, 20). An earlier study reported that contrast sensitivity decreases as visual field loss increases in glaucomatous eyes with visual acuity of 20/40 (logMAR 0.3) or better (21). However, their participants consisted of both glaucoma and glaucoma suspects; thus, whether contrast sensitivity is affected differently in POAG suspects only, warrants further investigations.

The evaluation of IOP is influenced by a thin central corneal thickness (CCT) thus, CCT is also a predictor of glaucoma (22, 23). Artificially low IOP in thin corneas can be missed, while IOP can be overestimated thick corneas where the patients may have normal IOP. CCT has been reported to vary between different glaucoma subtypes (24). Variation in CCT explains a substantial portion of the increased risk of glaucoma even after adjustment for IOP. However, the characteristic of CCT in POAG suspects and how it differs from visually normal patients is currently unknown.

Thus, the purpose of this study was to compare the contrast sensitivity score and central corneal thickness between POAG suspects and a visually normal (control) group of similar age. The comparison will determine if these structural and functional parameters are susceptible to changes in POAG suspects compared to their visually normal counterparts.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Ophthalmology Clinic, Hospital Kuala Lumpur, between September 2020 and January 2021. A verbal explanation and a written information sheet were provided to potential participants before their enrolment. All potential participants who agreed to participate signed the informed consent form. The study design and protocol were approved by Research Ethics Committee, Universiti Kebangsaan Malaysia (UKM PP/111/8/JEP-2020-788) and Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (KKM/NIHSEC/P20-1093(12)) and in accordance to the tenets of the Declaration of Helsinki.

Participants were divided into a POAG suspect group and a control group. The sample size was calculated using G*Power version 3.1.9.4 (25). To detect an effect size d=0.5 with 80% power (alpha=0.05, one-tailed), the total number of participants required for this study was 106.

The clinical findings in one or both eyes of an individual with an open anterior chamber angle that define a POAG-suspect patient were: an appearance of the optic disc or retinal nerve fibre layer (RNFL) that was suspicious for glaucomatous damage; or a visual field suspicious for glaucomatous damage in the absence of clinical signs of other optic neuropathies; or a consistently elevated IOP associated with normal appearance of the optic disc, RNFL, and visual field (26). If a patient had an angle 180 degrees or more of iridotrabecular contact, no peripheral anterior synechia, normal IOP, no optic nerve damage, and visual field defect, they were considered a Primary Angle Closure Suspect (PACS) and were excluded (8, 27). POAG suspects with vertical CDR>0.4 and IOP<22mmHg were selected in this study. Qualified and trained Medical Officer in Ophthalmology or Ophthalmologist made the diagnosis of glaucoma suspects. All glaucoma suspects were under ophthalmology follow-up and subjected to visual field and OCT assessments. Inclusion criteria for participants in the control group include a CDR ≤0.4 and IOP ≤21mmHg without any presence of other ocular comorbidities. Other inclusion criteria were age between 40 to 80 years old with corrected visual acuity of 6/12 and better, minimum of N6 for near vision, a refractive error between +2.00D to -6.00D and astigmatism <-3.00DC. Participants with uncontrolled systemic disease, diabetic retinopathy, maculopathy, age-related macular degeneration, posterior subcapsular cataract, post subcapsular opacities in pseudophakia and on anti-glaucoma medication were excluded. Those with IOP≥ 22mmHg which indicated ocular hypertension were also excluded. All participants had no history of corneal refractive surgery and ocular surface disorder including severe dry eyes.

Data related to the inclusion criteria were obtained from the patient's medical record. Visual acuity distance and near was measured on the same day. Refractive status was available either from the current medical record or determined on the same day. Contrast sensitivity was measured with the Pelli–Robson chart at 1 meter with corrected visual acuity and undilated pupil. Participants were asked to read the chart from the high to low contrast until the letters could not be seen. The change in contrast between groups of three letters was 0.15 log units. Each

correctly identified letter was assigned with a 0.05 log unit of CS. CS measurement was performed at a single location/room under constant illumination. Illumination on chart was~30 to 32ft.cd (foot-candle) measured with a light meter by Sper Scientific (model number 840021), and conducted when all the inclusion criteria were fulfilled. CCT record was readily available in the patient's medical record but primarily was measured on the same day using a hand-held pachymeter after the CS test. IOP was measured using an applanation tonometer, and CDR was estimated using a diagnostic lens during fundus assessment with the slit-lamp examination. The attending medical officer or Ophthalmologist measured the IOP and CDR.

All of the data were analysed using SPSS version 25. Descriptive statistics, including mean, standard deviation, and range, were used to calculate the numeric variables, including the clinical characteristic of the eyes. Frequencies (%) were used to illustrate the categorical variables such as gender and ethnicity. The study participants were categorised into two clinical groups; POAG suspect group and the control group. They were further stratified into four age groups; 40 to 49, 50 to 59, 60 to 69 and 70 to 80 years old. A two-way analysis of variance (ANOVA) was performed to determine any significant differences in CS and CCT between the clinical and age groups. Then, the Turkey post hoc test was used to determine significant differences between the four age groups and between the POAG suspect and control groups.

RESULTS

A total of 115 POAG suspects and 102 control individuals participated in this study. The participants' age ranged from 40 to 80 years old. The mean age of POAG suspects and control participants was not statistically different, being 59.91±9.84 and 60.04±10.83, respectively (t (217)=-0.095, p=0.93). Malay was the largest ethnic group, representing 53% of the participants, followed by ethnic Indian (26%) and ethnic Chinese (19%). There were 94 (43.3%) male and 123 (56.7%) female participants. Positive family history of glaucoma was found in 12.6% of the POAG suspects. The mean depression (MD) on the visual field testing of the glaucoma suspects was -1.49±2.80. The vertical cup-disc ratio (CDR) was significantly different between the POAG suspects and control group ((Z=-13.13, p<0.001). The IOP was not significantly different between the groups (Z=-0.283, p=0.777). As a whole, 34.4% of the study participants had clear crystalline lens, 63.3% had nuclear sclerosis and the remaining were psuedophakic. In the 40-49 year-olds, 80% had clear lens and 16% had nuclear sclerosis. Among the 50-59 year olds, 59.3% had nuclear sclerosis. The incidence of nuclear sclerosis increased to 96.7% and 100% in the 60-69 and 70-80 year-old groups, respectively. The visual acuity for right and left eyes of glaucoma suspects and the control group were not significantly different (F(1,211)=0.022, p=0.881. The refractive error (spherical equivalent) for the right and left eyes of glaucoma suspects and the control group were also not significantly different [F(1,211)=1.41, p=0.236]. Thus, data from the right eye w ere selected for subsequent analyses. The study participants' clinical characteristics are summarised in Table I.

Table I: Clinical characteristics of study participants

	POAG suspect	Control	P-value
Age	59.91±9.84	60.04±10.83	0.968
Gender (Male/Female)	55/60	39/63	0.155
Spherical Equivalent	-0.62±1.84	-0.14±1.30	0.206
Cylinder	-0.60±0.64	0.70±0.65	0.184
Distance VA right eye (logMAR)	0.11±0.09	0.10±0.09	0.213
Distance VA left eye (logMAR)	0.11±0.09	0.09±0.09	0.166
IOP	15.07±2.27	14.98±2.61	0.777
CDR (vertical)	0.62±0.10	0.32±0.04	<0.001

The mean of CS according to age group are shown in Table II. Glaucoma suspects generally had a lower CS compared to the control group. There was a significant effect of the clinical condition on CS [F(1,209)=5.409, p=0.02]. The effect of age on CS was also statistically significant [F(3,209)=20.419, p<0.001]. However, the interaction between age and the clinical condition was not statically significant [F(3,209)=0.815, p=0.49]. That is, the change in age did not influence the difference in mean CS between POAG suspects and the control group. A post hoc Tukey test showed that the CS scores of POAG suspects were significantly lower than the controls for the younger age groups (40 to 49 and 50 to 59; p<0.05) but not for the older age groups (60 to 69 and 70 to 80; p=0.70). The variance in CS due to age and the clinical condition was 22% (adjusted R2=0.22).

Table II: Comparison of contrast sensitivity (CS) score across age groups in POAG suspects and controls

Age Group	POAG suspect		Control	
	N	Mean ± SD	N	Mean ± SD
40 to 49	22	1.67 ± 0.08	21	1.72 ± 0.09
50 to 59	29	1.59 ± 0.11	22	1.64 ± 0.08
60 to 69	43	1.59 ± 0.10	36	1.59 ± 0.07
70 to 80	23	1.53 ± 0.12	23	1.54 ± 0.12
Total	115	1.59 ± 0.11	102	1.62 ± 0.11

The mean of CCT according to age groups are shown in Table III. There was no significant effect of clinical condition on CCT [F(3,209)= 0.754, p=0.39]. However, there was a significant effect of age on CCT [F(3,209)= 3.789, p=0.01]. No significant interaction was found between age and clinical condition [F(3,209)=0.205, p=0.90]. That is, the change in CCT due to age is similar between those who were POAG suspects and controls.

Table III: Comparison of central corneal thickness (CCT) across age groups in POAG suspects and controls

Age Group	POAG suspect		Control	
	N	Mean ± SD (µm)	N	Mean ± SD (µm)
40 to 49	22	552.91 ± 28.77	21	552.48 ± 30.11
50 to 59	29	539.79 ± 33.34	22	530.23 ± 39.3
60 to 69	43	532.21 ± 30.80	36	531.11 ± 32.47
70 to 80	23	5.39.35 ± 31.79	23	534.09 ± 42.17
Total	115	539.44 ± 31.72	102	535.99 ± 36.67

DISCUSSION

Glaucoma patients are often diagnosed through a preliminary examination in optometry practice, opportunistic findings during symptomatic eye diseases evaluation, or during diabetic screening fundus photography. In practices with minimal facilities such as an ophthalmoscope and a fundus camera, glaucoma suspects are commonly identified by an enlarged CDR, together with other risk factors such as a positive family history and an elevated IOP. As glaucoma suspects may have one or some glaucoma risk factors, they have higher chances for normal visual function to be preserved from further impairment if glaucoma diagnosis is achieved as early as possible. However, the diagnosis is sometimes delayed until visual field defects are detected with standard automated perimetry.

In early or moderate glaucoma patient with VA 6/9 or better, the main symptoms reported include needing more light, blurry vision, and seeing glare (28). The decreasing quality of vision is often noticed by the patients, but not explained by their clinically good VA (29). We found that overall, glaucoma suspects had reduced CS than visually normal participants. The difference was more pronounced in the younger age groups (between 40 to 59 years old). Studies have shown that CS declines with age at all spatial frequencies (19, 30) and with pathology such as cataract (31) where cataract severity is correlated with decreasing VA (32, 33). In our study, mild nucleus sclerosis with good VA was seen in the majority of our older age group eyes due to age-related changes in the crystalline lens. Although all eyes had a vision of at least 0.2 logMAR (Snellen 6/9), it was almost impossible to select older-aged participants with completely clear crystalline lens. Indeed, early nucleus sclerosis rarely causes a reduction of VA, while CS would be more affected by early posterior subcapsular and cortical cataract at a spatial frequency higher than 6 cycles per degree. Nevertheless, an early nuclear cataract may cause a significant reduction in CS but predominantly in patients who are 60 years and older (32). Smaller pupil size, increased lenticular absorption and scattering of light by crystalline lens affect the contrast of the image on the retina and retinal illumination in the elderly (34). Thus, older patients with smaller pupil size would have lower retinal illuminance and a decrease in CS (35, 36). Although pupil size was not measured in this study, it can be assumed that smaller pupil size had caused a further reduction in CS in older participants, with pupil size reportedly being smaller in eyes with glaucoma (37). Thus, it is stipulated that the reduction in CS in younger glaucoma suspects in this study, compared to the age-matched control group, was unlikely due to pathological changes such as cataracts. It has been reported that young glaucoma patients had a thicker macular inner retinal layer, suggesting transient gliosis that were associated with reduced CS (38).

We also found that CCT to be reduced with age. However, the change in CCT across age groups was similar for both glaucoma suspect and normal participants. Indeed, it has been shown that ageing causes reduction in CCT due to decrease in corneal volume in the central 10 mm (39). The association of larger CDR, elevated IOP, and thinner CCT with a higher risk of glaucoma have been studied extensively (23, 40-43). IOP may be affected by CCT thus influences the diagnosis and management of glaucoma. In addition, it is affected by many internal and environmental factors such as blood pressure, daily activities and caffeine or alcohol intake (44). Although studies have shown that CCT of 555 µm or less had a 3-fold greater risk of developing glaucoma in ocular hypertensive patients (38), CCT measurements may not fully differentiate POAG glaucoma suspects and visually normal patients in our sample of participants.

A limitation of this study is that CCT measurement was not controlled during data collection. The participants were not gender-matched, where there was a slightly higher percentage of females than males. As it has been speculated that sex hormones could influence intraocular pressure and blood flow (45), the effect of sex on the studies parameters would be an interesting direction for future studies. In addition, there reported results could also be affected by the participants' ethnicity. Further studies need to be conducted to explore how CS and CCT are affected by other glaucoma risk factors such as IOP and CDR in patients suspected of having primary open angle glaucoma and primary angle closure glaucoma.

CONCLUSION

Contrast sensitivity measurement is potentially useful

to be integrated in routine glaucoma investigations for POAG suspect patients, especially those younger than 60 years old. On the other hand, the central corneal thickness may not differentiate between POAG suspects and visually normal individuals.

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