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Peripapillary Choroidal Thickness Measurement in Primary Open-angle Glaucoma Patients Using Optical Coherence Tomography

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Abstract

Background: Glaucoma is one of the most typical causes of irreversible visual impairment in the globe, primary open-angle glaucoma (POAG) is the most common subtype of the disease and can impact the quality of life by affecting the visual field even if the patient is unaware of his diagnosis.

Aim of the work: To measure the peripapillary choroidal thickness (PCT) in POAG patients and to assess the correlation between peripapillary choroidal thickness and the degree of the condition using enhanced depth imaging optical coherence tomography.

Patients and methods: A prospective, observational case–control study was carried out from March 2021 till March 2022 at Al-Azhar University Hospitals involving 40 eyes of twenty-four adult subjects, 20 eyes of 10 healthy persons, and 20 eyes of 14 patients previously diagnosed with POAG.

Results: Forty eyes of 24 subjects were enrolled in this study, with a mean age of 56.16 years old. 41.66% of patients were males [10/24], while females were 58.33% [14/24]. PCT in the glaucoma group was less than in the control group; however, the difference was statistically insignificant.

Conclusion: No significant correlation between PCT in POAG and the severity of the condition so peripapillary choroidal thickness has no role in the diagnosis or follow-up of primary open-angle glaucoma.

Keywords: Choroid, Coherence, Glaucoma, Optical, Tomography

1. Introduction

Glaucoma is a category of diseases that have vision loss in common. Owing to high intraocular pressure, this lack in vision is caused by damage to the optic nerve. The disease's mechanisms are well established; however why an individual develops glaucoma remains unknown in most cases.¹

POAG is a progressive, usually bilateral, progressive optic neuropathy that develops after the age of 40 years. It is the world's second most common cause of irreversible visual impairment. POAG is associated with progressive retinal ganglion cell loss, characterized by optic disc excavation and

associated with common visual field defects. The principal risk factor for POAG is raised intraocular pressure.²

The diagnosis and monitoring of POAG is based on structural alteration findings, clinical optic disc examination completed by imaging tests as OCT and functional changes by visual field tests. Decreasing intraocular pressure with anti-glaucomatous medications, laser therapy or surgical treatment is the only successful treatment to delay the progression of POAG.²

The choroid is part of the uveal tract and also includes connective tissue and melanin pigment as a highly vascularized bed. Due to the function of the

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choroid in the blood supply of the optic nerve head (ONH) in the anterior laminar and prelaminar regions, the peripapillary choroid may be a valid subject for research in glaucoma cases.³

Since the peripapillary choroidal branches are the primary source of blood supply to this area, it is assumed that the incidence of glaucomatous optic neuropathy (GON) could involve irregular choroid circulation. It is especially difficult to examine, however, since it is situated underneath the retinal pigment epithelium (RPE).⁴

OCT is a noninvasive investigation for cross-sectional imaging of tissues. Typically, light is used in the near-infrared spectral range, which has an ability to penetrate tissue for several hundred microns. With an interferometric set-up, the back-scattered light is calculated to reconstruct the sample's depth profile at the selected place. A scanning OCT beam enables cross-sectional images of the tissue structure to be acquired.⁵

OCT is a high definition device for imaging glaucoma cases which is capable of retinal nerve fiber layer (RNFL) and ONH measurements. This kind of investigations has developed a safe ethnic-specific database on the basis of which normal probability map is given for the clinical diagnosis of POAG, however, can only represent the normal probability of each selected region, rather than the probability of a particular person developing glaucoma.⁶

This study aimed to measure PCT in POAG patients and to assess the correlation between PCTs and the degree of the condition using EDI-OCT.

2. Patients and methods

2.1. Subjects

A prospective, observational case control study was carried out from March, 2021 till March, 2022 at Al-Azhar University Hospitals involving 40 eyes of 24 adult subjects, These cases were divided into 2 groups, The first group (**Control group**): 20 eyes of 10 healthy people with no history of systemic or ocular diseases, And the second group (**Glaucoma group**): 20 eyes of 14 patients previously diagnosed with POAG, controlled medically, with the following inclusion and exclusion criteria.

2.2. Inclusion criteria

For POAG patients their age must be >40, on gonioscopy examination the anterior chamber angle must be opened (>grade 2), IOP rise without secondary causes (>21 mm Hg), were receiving IOP-lowering therapy, and glaucomatous optic

neuropathy should be confirmed (detected as a vertical cup/disc ratio (CDR) > 0.7 and/or cup/disc asymmetry >0.2 and/or focal notching).

Visual field defects on static automated perimetry in the form of glaucoma hemifield test outside normal limits, abnormal pattern standard deviation of P-value <5% in the normal individuals, and achieving reliability criteria of the test (fixation losses <20%, false positives < 33%, and/or false negatives ≤33%).

For each eye with POAG, a healthy subject was enrolled and served as a control with no previous history of ocular condition except cataract not affecting the OCT image quality, no intraocular surgery, and IOP <21 mm Hg.

2.3. Exclusion criteria

Candidates were excluded if age was <40 and if refractive error was > -6.00 diopter (D), +6.00 D, or astigmatism amplitude more than 3.00 D. Also cases with retinal conditions were excluded. Other causes such as ocular trauma, neuro-ophthalmological disease that could alter the analysis of the visual field. Finally cases with media opacity (vitreous hemorrhage, significant cataract or corneal opacity) that interfere with fundus examination and OCT interpretation, or cases with recent eye surgery (within 2 months) were excluded.

A written informed consent according to the Declaration of Helsinki was acquired from each participant before enrollment. During this study, all applicable institutional rules on the ethical employment of human participants were followed.

2.4. Methods

Complete ophthalmic, medical and family history was taken, All cases were submitted to a general ophthalmologic examination including non-cycloplegic refraction by usage of an auto refractometer (ARK-310; NIDEK, Aichi, Japan)- Refraction data were converted to spherical equivalents, best corrected visual acuity (BCVA) measurement by Snellen's visual acuity chart, which was converted into Logarithm of Minimum Angle of Resolution (LogMAR) for statistical analysis, stereoscopic fundus examination through fully dilated pupil using slit lamp biomicroscopy with +90D lens to detect glaucomatous optic disc changes [cupping, asymmetrical cupping difference >0.2, notching, kinking of vessels, NFL defects and peripapillary atrophy], and IOP assessment by Goldmann applanation tonometer.

Standard automated perimetry (SAP) with Humphrey Visual Field Analyser II (Carl Zeiss Meditec, Dublin, CA) was performed using the Swedish Interactive Thresholding algorithm standard 24–2 test pattern. Pattern standard deviation (PSD), Mean Deviation (MD) and field defects were noted.

Optical Coherence Tomography Scanning with Spectralis SD OCT system (Heidelberg Engineering, Heidelberg, Germany). was performed using the built-in NFL circle scan protocol of 3.4 mm around optic disc with enhanced depth imaging technique. Mydriatics were used before image capturing. If the image quality was inadequate, the scans were discarded. Patients were instructed to fixate on the intrinsic fixation target during the whole process of OCT scanning. If the subject was not fixating enough on the fixation target and the center of image was not on center of the fovea, manual correction was made. All the scans were taken by a single experienced doctor (Fig. 1).

Determination of peripapillary RNFL thickness and peripapillary choroidal Thickness: The RNFL thickness was automatically measured and analyzed in comparison to its normative database. The PCT was measured manually in all quadrants (temporal, superior, nasal and inferior) starting from the outer border of the hyperreflective line corresponding to the RPE to the inner border of the sclera (choroid sclera interface). The choroid was measured by two neutral examiners who were unaware to the condition, and then their measurements were averaged (Fig. 2). shows EDI-OCT of left eye of a 36 years old

female patient in this study showing peripapillary RNFL and choroidal thickness measurement in inferior, superior, nasal, temporal quadrants.

2.5. Statistical methods

Statistical package for the Social Sciences (SPSS) version 28 was used to code and input the data (IBM Corp., Armonk, NY, USA). For quantitative variables, mean and standard deviations were used to describe the data. But for categorical variables, frequencies (number of cases) and relative frequencies (percentages) were used. Unpaired *t* test was used in comparisons between groups in normally distributed quantitative variables while in non-normally distributed quantitative variables nonparametric Mann–Whitney test was used. For comparing categorical data, Chi square (χ^2) test was employed. But when the expected frequency was less than 5 exact test was performed. Spearman correlation coefficient was used to analyze correlations between quantitative variables, and *P* values less than 0.05 were considered as statistically significant.

3. Results

A total of 40 eyes of 24 subjects were enrolled in this observational study, with mean age of 56.16 years old. The mean age of control group was 52.20 ± 5.96 Years old versus 56.80 ± 8.64 years old in glaucoma group. Females were more in both control and glaucoma groups. Males were 41.66% of



Fig. 1. The Spectralis Heidelberg OCT device used in this study.

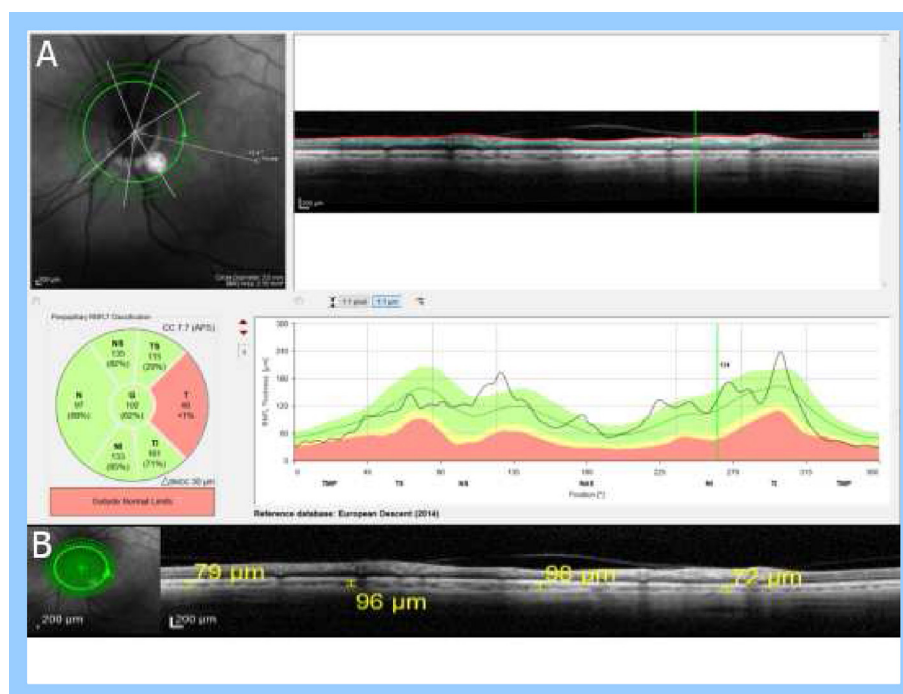


Fig. 2. EDI-OCT of the left eye of a patient in this study showing (A) average peripapillary RNFL thickness (B) average peripapillary choroidal thickness.

patients [10/24], while females were 58.33% [14/24]. These cases were divided into control group (20 eyes of 10 patients) and glaucoma group (20 eyes of 14 patients).

There was no statistically significant difference between the average ages of both groups, neither statistically significant difference between the average numbers of both sexes in both groups. And patient's demographics are shown in Table 1.

The mean peripapillary choroidal thickness in different quadrants was less in glaucoma than controls. These differences were statistically non-significant in all quadrants (P value > 0.05). (Table 2).

On this study we find no correlation between MD of visual field analysis and PCT in different quadrants (Temporal, Superior, Nasal, and Inferior) in glaucoma group (Table 3).

However, we found a significant negative correlation between PSD of visual field analysis and PCT

in inferior quadrant with correlation coefficient (-0.770) (P value = < 0.001). (Table 4).

This study in glaucoma group found a significant negative correlation between the average peripapillary RNFL thicknesses in superior, nasal, and inferior quadrants and the average peripapillary choroidal thickness in the corresponding quadrants with correlation coefficient (-0.571 , -0.661 , -0.588 , respectively) (P value = 0.008 , 0.002 , 0.006 , respectively). (Table 5).

4. Discussion

It is unclear how the choroid fits into the extensive network of factors that have a role in the etiology of GON. The thickness of the choroid in glaucomatous eyes has been measured in several investigations utilising histology or in vivo imaging methods.

The contradictory findings of those studies, together with current breakthroughs in imaging of the ocular posterior region, especially SD-OCT, prompted a re-evaluation of the interconnection between choroidal thickness and glaucoma.

4.1. According to our study

PCT in glaucoma group was less than control group, but this difference was statistically insignificant with p -value (0.932 , 0.159 , 0.216 , and 0.059) in

Table 1. Patient's demographics data of both groups according to age and sex.

	Controls		Glaucoma		P value
	Mean	SD	Mean	SD	
Age	52.20	5.96	56.80	8.64	0.057
	Count	%	Count	%	
Sex					
Females	6	60.0%	8	57.1%	1
Males	4	40.0%	6	42.9%	

Table 2. The average peripapillary choroidal thickness in different quadrants (temporal, superior, nasal, and inferior) in both controls and glaucoma groups.

	Controls		Glaucoma		P-value
	Mean	SD	Mean	SD	
Temporal Peripapillary Choroidal Thickness	203.70	12.10	126.10	45.29	0.932
Superior Peripapillary Choroidal Thickness	224.80	11.95	151.10	54.01	0.159
Nasal Peripapillary Choroidal Thickness	229.80	26.98	147.30	37.08	0.216
Inferior Peripapillary Choroidal Thickness	197.90	13.61	120.00	36.61	0.059

Table 3. Correlation of MD of visual field analysis with PCT in different quadrants (temporal, superior, nasal, and inferior).

Glaucoma	Visual Field Mean Deviation (MD)
Temporal Peripapillary Choroidal Thickness	
r	0.164
P-value	0.491
N	20
Superior Peripapillary Choroidal Thickness	
r	0.370
P-value	0.109
N	20
Nasal Peripapillary Choroidal Thickness	
r	0.406
P-value	0.076
N	20
Inferior Peripapillary Choroidal Thickness	
r	0.345
P-value	0.136
N	20

r: correlation coefficient.

(temporal, superior, nasal and inferior) quadrants respectively.

Also, This study in glaucoma group found a significant negative correlation between the average peripapillary RNFL thicknesses in superior, nasal, and inferior quadrants and the average PCT in the

Table 4. Correlation of PSD of visual field analysis with PCT in different quadrants (temporal, superior, nasal, and inferior).

Glaucoma	PSD
Temporal Peripapillary Choroidal Thickness	
r	-0.261
P value	0.267
N	20
Superior Peripapillary Choroidal Thickness	
r	-0.358
P value	0.122
N	20
Nasal Peripapillary Choroidal Thickness	
r	-0.430
P value	0.058
N	20
Inferior Peripapillary Choroidal Thickness	
r	-0.770
P value	<0.001
N	20

r: correlation coefficient.

corresponding quadrants with correlation coefficient (-0.571, -0.661, -0.588, respectively) (P value = 0.008, 0.002, 0.006, respectively).

There was nonsignificant correlation between MD of visual field and peripapillary choroidal thickness in all quadrants.

Also we found significant negative correlation between PSD of visual field and peripapillary choroidal thickness in all quadrants.

The primary conclusion of our study is thicker peripapillary choroid in normal than POAG, but this difference was not statistically significant.

So our study results support the findings from previous studies on peripapillary choroidal thickness and glaucoma as follows:

In 2011, a retrospective study using Spectralis SD-OCT, Ehrlich J. and his colleagues⁷ measured the circumpapillary choroidal thickness and didn't find any correlation between RNFL thickness and choroidal thickness in corresponding quadrants in eyes with POAG or reduced choroidal thickness in those eyes. A significant correlation between the average NFL thickness in the nasal quadrant and PCT in the nasal quadrant was discovered, in contrast to our findings, which showed a significant negative correlation between average NFL and average CT in nasal quadrant in the glaucoma group (correlation coefficient of -0.661, P value = 0.002).

While in the same year Maul E.A. and his colleagues⁸ used EDI-OCT to quantify choroidal thickness in a sample of glaucoma suspects and glaucoma patients, they discovered no correlation between choroidal thickness and the severity of glaucomatous damage.

Table 5. Relationship between RNFL and choroidal thickness in different quadrants (temporal, superior, nasal, and inferior) in glaucoma group.

Choroidal Thickness	RNFL Thickness	r	P-value
Temporal	Temporal	0.091	0.702
Superior	Superior	-0.571	0.008
Nasal	Nasal	-0.661	0.002
Inferior	Inferior	-0.588	0.006

r: correlation coefficient.

Wang Y.X. and his colleagues⁹, also Zhang Y.Q. and his colleagues¹⁰ both found no evidence of a relationship between PCT and POAG in their meta-analyses.

In 2011, Mwanza J. and his colleagues¹¹ announced their results with imaging of the choroid with Spectralis SD-OCT in POAG and normal-tension glaucoma (NTG) and normal healthy subjects. They supported that axial length and age had the greatest effects on choroidal thickness (the more the age or the axial length, the more the choroidal thinning). Regarding choroidal thickness, the investigators did not discover any significant differences among the three groups. The same findings were supported in a subsequent study conducted by the same author in 2012 on patients with unilateral advanced glaucoma. This concludes that neither choroidal thickness nor glaucoma severity is related to glaucoma.

In 2014, Hosseini H. and colleagues¹² presented a study on macular and PCT in patients with perimetric glaucoma. They found no significant difference between patients with open angle glaucoma and non-glaucomatous individuals in subfoveal choroidal thickness. They extended the investigations into the peripapillary region, where they found that, with the exception of the temporal region, choroidal thickness was similar in glaucomatous and control eyes, which is consistent with the current results. These results might suggest that open angle glaucoma does not significantly involve or alter choroidal blood circulation. However, because the choroid is extremely high dynamic vascular tissue, only anatomic measurements, such as choroidal thickness, might not be able to fully capture changing hemodynamic physiology in a variety of ocular conditions. Peripapillary choroid flow patterns, in particular, would be of great value in monitoring glaucoma.

According to in 2012, Arora K. and his colleagues¹³ choroidal thickness was not significantly correlated with the degree of GON as determined by cup/disc ratio or MD of visual field analysis. Similar findings were made by Hosseini H. with his colleagues¹², and Mwanza J. with his colleagues¹⁴ who found no correlation between choroidal thickness and the degree of glaucoma (as measured by RNFL thickness and MD). Regarding the association between CT and MD, these findings are similar with the current findings, but not with PSD, where there was a negative correlation between CT & PSD.

The findings by the above-mentioned studies are consistent with results of this study regarding the lack of a significant difference between the PCT in POAG and normal eyes.

4.2. In comparison with our study

In 2011, a study including 65 healthy eyes and 78 POAG eyes, Bron A. with his colleagues¹⁵ found that PCT was thinner in POAG patients than in normal controls. Further, a meta-analysis in 2016 by Lin Z. and his colleagues¹⁶ demonstrated that mean PCT in POAG was significantly lower than in healthy controls, providing possible evidence for the vascular theory of glaucoma and raising the possibility that retrobulbar ischemia may have an effect on the ONH. The significantly smaller sample size may be the reason why these results differ from those of the current study.

Regarding NTG, Hirooka K. and his colleagues⁷ showed that in comparison to healthy individuals, the mean PCT was significantly thinner in the NTG eyes. Additionally, they found that the inferonasal, inferior, or inferotemporal quadrants of the PCT of the NTG patients decreased along with a corresponding worsening of the GHT, So according to these findings, that the choroid was thinner in NTG than normal whereas in POAG was neither increased nor decreased when compared to normal may suggest that altered choroidal blood supply is an important factor contributing to the higher incidence of GON in NTG patients compared to POAG patients.

Expected restrictions of this study maybe that a cross-sectional study cannot show long term changes, Also the sample size is relatively small, And peripapillary choroidal thickness was only measured without measuring the subfoveal choroidal thickness.

5. Conclusion

No significant correlation between PCT in POAG and degree of the condition, so PCT has no role in diagnosis or follow up of POAG.

Authorship

All authors have a great participation to the article.

Conflicts of Interest

None declared.

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