Ophthalmology

Relationship between Central Corneal Thickness, Intra-Ocular Pressure, Retinal Nerve Fiber Layer Thickness and Ganglion Cell Layer Thickness in Primary Open Angle Glaucoma

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ABSTRACT

Background: Primary open angle glaucoma is a multifactorial disorder characterised by the death of retinal ganglion cells, which results in a characteristic optic neuropathy and concomitant visual field reduction.
Aim of The Work: to determine the association between central corneal thickness, intraocular pressure, peri-papillary retinal nerve fiber layer thickness, and ganglion cell layer thickness in patients with primary open angle glaucoma.
Patients and Methods: A cross-sectional observational study included 60 eyes of 36 patients with primary open angle glaucoma conducted at the Ophthalmology Department, Al Azhar University Hospitals between April 2020 and April 2021.
Results: We found a significant negative correlation between corrected IOP Versus total, superior and inferior GCL+ in the studied POAG patients. There was also significant negative correlation between corrected IOP Vs. total, superior and inferior RNFL in the studied POAG patients. There is no significant correlation between CCT vs. IOP, macular GCL, Total RNFL or superior RNFL thickness while there was a positive correlation detected between CCT and inferior RNFL in the studied POAG cases.
Conclusion: In the studied POAG cases, we found positive associations between CCT and inferior RNFL, but no significant association between CCT and IOP, macular GCL, Total RNFL, or superior RNFL thickness.

Keywords: *Open angle glaucoma; Retinal nerve fiber layer thickness; Ganglion Cell Layer Thickness; Corneal Thickness.*

INTRODUCTION

Primary open angle glaucoma is a multifactorial disorder characterised by the death of retinal ganglion cells, which results in a characteristic optic neuropathy and concomitant visual field reduction. Despite the fact that the specific pathophysiology of open angle glaucoma is unknown, increased intraocular pressure (IOP) is considered the most important risk factor for the development and progression of glaucomatous neuropathy. [1]
The CCT, as well as the IOP, are important for assessing glaucoma since a low CCT will result in an underestimation of IOP, which will impact the glaucoma prognosis.[2]
Throughout the progression of glaucoma, the loss of retinal ganglion cells (RGCs) has been identified as a fundamental and important pathophysiological process. According to various histological studies, Changes in RGC shape and cell density occur before clinically noticeable VF loss. As a result, detecting RGC depletion early is crucial for diagnosing glaucoma and monitoring its progression. The axons of RGCs leave the cells and form the optic nerve, which is made up of retinal nerve fibers. As a result, the circum-papillary retinal nerve fiber layer

(cRNFL) thickness has been used to assess the severity of glaucoma damage.[3]

In healthy patients, macular thickness does not change over time, and lower macular thickness is mostly indicative of glaucoma. Furthermore, researches suggests that unlike the ganglion cells in the entire retina, the ganglion cell population in the macula is generally steady among normals. On the other hand, The Optic nerve varies individually in size, shape, slanting, and other characteristics. [4]

PATIENTS AND METHODS

A set of 60 eyes of 36 individuals with primary open angle glaucoma were included in this cross-sectional observational study. It was conducted at the Ophthalmology Department, Al Azhar University Hospitals between April 2020 and April 2021

The patient's inclusion and exclusion criteria, Inclusion criteria: Patients from either sex aged 35 and above, patients with mild to severe primary open angle glaucoma and not controlled by medical treatment and glaucomatous patients with cataract not obscuring fundus view. **Exclusion criteria**:

Secondary glaucoma, non-glaucomatous cause of optic neuropathy, history of previous corneal disease or trauma, patient with other retinal disease like diabetic neuropathy and high myopia, patients with optic disc anomalies like papilledema, history of previous ocular trauma, patients with dense cataract obscuring fundus view and history of previous Intra-Ocular Surgery.

Methodology: Complete medical history including previous ocular trauma, medications or surgeries. Visual acuity assessment (Best corrected visual acuity) using Snellen's acuity chart and expressed in Decimal notation. Ophthalmological examination: slit lamp biomicroscopy for assessment of the anterior segment and fundus biomicroscopy for assessment of the optic nerve head. Pentacam (by Sirius CSO, Firenze, Italy) For assessing central corneal thickness, Tonometry (by Goldmann applanation tonometry) for assessing IOP, OCT (by DRI OCT Tritonplus, Topcon, Japan) for assessing Macular Ganglion cell layer thickness and Peri-papillary Retinal nerve fiber layer thickness.

Statistical methods: Data analysis was done by IBM SPSS statistics (V. 26.0, IBM Corp., USA, 2019). Date expressed as Mean ± STDEV for quantitative parametric normally distributed measurements in addition to both number and percentage for categorical data, for parametric data, the Pearson correlation test is used to investigate the possible relation between two variables within each group. The probability of error was considered significant at 0.05, whereas it was very significant at 0.01 and 0.001.

RESULTS

Parameters		Primary Open Angle Glaucoma (POAG) patients No.= 60
Intra-Ocular Pressure (IOP)	Mean± STDEV	26.98 ± 2.801
	Range	21.0 – 34.0
Central Corneal Thickness (CCT)	Mean± STDEV	532.62 ± 25.05
	Range	475.0 – 589.0
Corrected Intra-Ocular Pressure (Corrected IOP)	Mean± STDEV	27.75 ± 2.99
	Range	22.0 – 35.0
Best Corrected Visual Acuity (BCVA) in Decimal	Mean± STDEV	0.175 ± 0.094
	Range	0.016 – 0.33

Table 1: Summary of Intra-Ocular Pressure (IOP), Central Corneal Thickness (CCT), Corrected IOP and Best Corrected Visual Acuity (BCVA) in decimal notation in patients of Primary Open Angle Glaucoma (POAG).

The mean IOP of the studied POAG patients before treatment was 26.98 ± 2.801 (Mean ± STDEV) with range from 21 to 34 mmHg while the mean corrected IOP of the studied POAG patients was 27.75 ± 2.99 (Mean ± STDEV) with range from 22 to 35mmHg. The mean CCT of the studied POAG patients was 532.62 ± 25.05 (Mean ± STDEV) with range from 475 to 589 microns. The mean BCVA in Decimal was 0.175 ± 0.094 (Mean ± STDEV). Table (1)

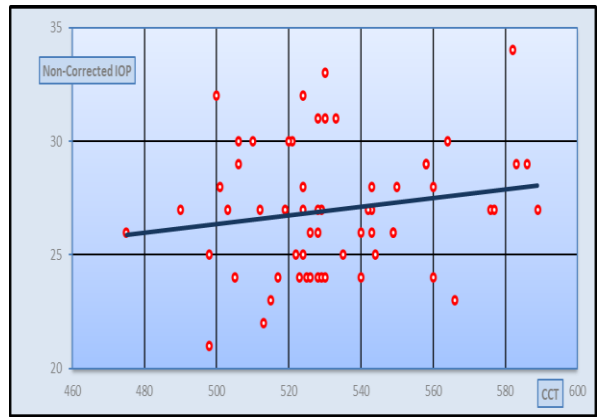| Parameters		Primary Open Angle Glaucoma (POAG) patients No.= 60
Superior Retinal Nerve Fiber Layer (Superior RNFL)	Mean± STDEV	107.43± 32.8
	Range	24– 175.0
Inferior Retinal Nerve Fiber Layer (Inferior RNFL)	Mean± STDEV	111.92 ± 31.66
	Range	32.0 – 163.0
Total Retinal Nerve Fiber Layer (Total RNFL)	Mean± STDEV	90.23± 20.85
	Range	31.0 – 122.0

Table 2: Summary of Retinal Nerve Fiber Layer (RNFL) in patients of Primary Open Angle Glaucoma (POAG).

The mean superior retinal nerve fiber layer thickness of the studied POAG patients was 107.43± 32.8 (Mean ± STDEV) with range from 24 to 175 while the mean of the inferior retinal nerve fiber layer thickness of the studied POAG patients was 111.92 ± 31.66 (Mean ± STDEV) with range from 32 to 163. The mean total retinal nerve fiber layer thickness of the studied POAG patients was 90.23± 20.85 (Mean ± STDEV) with range from 31 to 122. Table (2)

| Parameters		Primary Open Angle Glaucoma (POAG) patients No.= 60
Superior ganglion cell layer (Superior GCL)	Mean± STDEV	59.6 ± 7.54
	Range	42.0 – 75.0
Inferior ganglion cell layer (Inferior GCL)	Mean± STDEV	59.68 ± 8.016
	Range	41.0 – 74.0
Total ganglion cell layer (Total GCL)	Mean± STDEV	59.63 ± 7.36
	Range	43.0 – 74.0

Table 3: Summary of ganglion cell layer (GCL) thickness in patients of Primary Open Angle Glaucoma (POAG).

The mean superior ganglion Cell layer thickness of the studied POAG patients was 59.6 ± 7.54 (Mean ± STDEV) while the mean inferior ganglion Cell layer thickness of the studied POAG patients was 59.68 ± 8.016 (Mean ± STDEV). The mean total ganglion Cell layer thickness of the studied POAG patients was 59.63 ± 7.36 (Mean ± STDEV). Table (3)


Fig. 1: Correlation between Intra-Ocular Pressure (IOP) and Central Corneal Thickness (CCT) in the studied Primary Open Angle Glaucoma (POAG) patient

There was no significant correlation between Intra Ocular Pressure & Central Corneal Thickness (r= 0.17, p= 0.23) with slight tendency toward positive correlation. Figure (1)
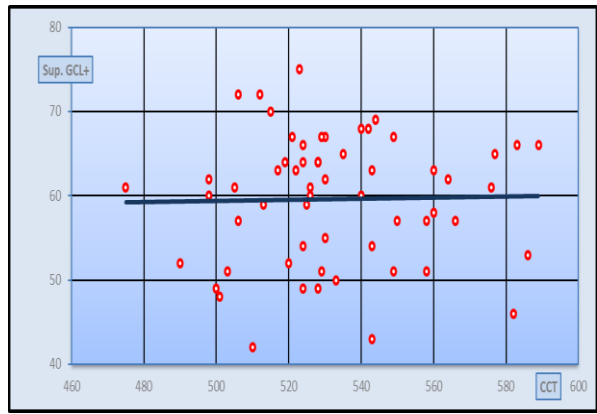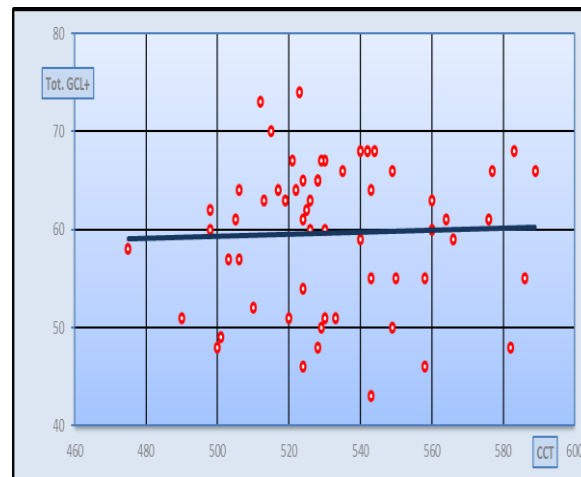

Fig. 2: Correlation between CCT & superior GCL in the studied POAG patients.   There was no significant correlation between CCT & superior GCL (r= 0.02, p= 0.88).

There was no significant correlation between Central Corneal Thickness & superior ganglion Cell layer thickness (r= 0.02, p= 0.88). Figure (2)
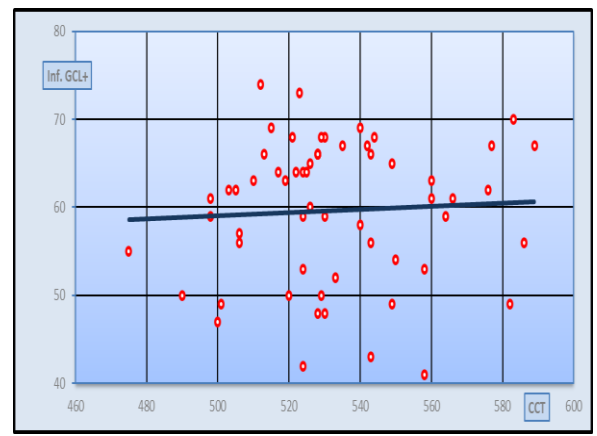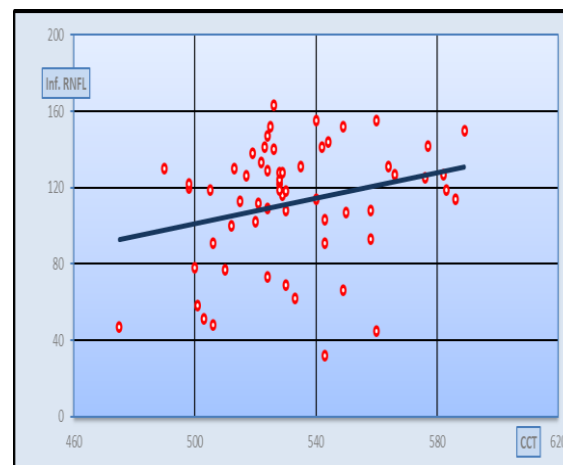

Fig. 3: Correlation between CCT & inferior GCL in the studied POAG patients.

There was no significant correlation between Central Corneal Thickness & inferior ganglion Cell layer thickness (r= 0.06, p= 0.67). Figure (3)

Fig. 4: Correlation between CCT & total GCL in the studied POAG patients.

There was no significant correlation between Central Corneal Thickness & total ganglion Cell layer thickness (r= 0.04, p= 0.79). Figure (4)

Fig. 5: Correlation between CCT & inferior RNFL in the studied POAG patients.

There was significant positive correlation between Central Corneal Thickness & inferior retinal nerve fiber layer thickness (r= 0.27, p= 0.04). Figure (5)

DISCUSSION

Despite the fact that CCT, GCL, and RNFL were significant indicators for glaucoma, the results were negative, that is not surprising considering their anatomical and physiological independence. Corneal thickness, on the other hand, is a well-known indicator of the eye's overall structure and biochemical features so CCT is a significant indicator for the progression of glaucoma.[5]

The aim of the current study is to assess the relationship between central corneal thickness, intra ocular pressure, retinal nerve fiber layer thickness and ganglion cell layer thickness in patients with primary open angle glaucoma.

This cross-sectional observational study was carried out on 60 eyes of 36 patients with primary open angle glaucoma at the Ophthalmology Department, Al Azhar University Hospitals, the study was carried out over a period of 12 months.

In the case of glaucoma, CCT is a significant factor. Despite its effect on IOP measurement, literatures have sparked a debate about its impact on glaucoma-related variables.[6]

Our results shows that the mean IOP of the studied POAG patients was 26.98 ± 2.801 with range from 21 to 34 mmHg while the mean corrected IOP of the studied POAG patients was 27.75 ± 2.99 with range from 22 to 35mmHg, the mean CCT of the studied POAG patients was 532.62 ± 25.05 with range from 475 to 589 microns, and the mean BCVA in Decimal was 0.175 ± 0.094.

In accordance to our results the study by Mahadevan et al., They found that the mean IOP was 23.48±2.47 (range: 22.8-24.08) mmHg and the mean CCT was 553.81±38.29 (range: 544.51-563.11) μm. There is high significant difference between the studied groups regarding IOP and No significant difference was detected in the CCT and RNFL values between the POAG and control groups. [7]

In contrary with our results Mohammed et al., observed that the IOP was found to be between 10 and 18 mmHg. CCT was 525.5±40.7 m on average. There were no significant variations in CCT or IOP between the right and left eyes (P>0.05). [6]

Our results shows that there was no noticeable relationship between IOP & CCT (r= 0.168, p= 0.229).

In contrary with our results Mohammed et al., They reported the presence of a strong positive association between CCT and IOP; patients with thick cornea had higher IOP than those with thinner corneas. [6]

The present work showed that the mean superior RNFL of the studied POAG patients was 107.43± 32.80 with range from 24 to 175 while the mean inferior RNFL of the studied POAG patients was 111.92 ± 31.66 with range from 32 to 163. The mean total RNFL of the studied POAG patients was 90.23± 20.85 with range from 31 to 122.

Our results revealed that there was no significant correlation between CCT & superior RNFL (r= 0.186, p= 0.154). Also, there was significant positive correlation between CCT & inferior RNFL (r= 0.266, p= 0.04). As well, there was no significant correlation between CCT & total RNFL (r= 0.23, p= 0.077).

In agreement with our findings Al Saad et al., revealed that there was no statistically significant association between CCT and RNFL (P= 0.285). despite that CCT, GCL, and RNFL were significant indicators for glaucoma, the results were negative, that is not surprising considering their anatomical and physiological independence. Also, they found statistically significant change between RNFL and the cases ages (P= 0.045). [7]

In contrast with our results the study of Mohammed et al., reported that CCT was the statistically significant predictor for the RNFL (P< 0.05). Also, they revealed nearly the same value of the mean total RNFL which was 87.2±16.8 (range: 43.63–122.06). [6]

Mansoori et al., made another study on an Indian population indicated that the average RNFL was around 114 microns, which was significantly higher than our findings. The RNFL parameters were unaffected by gender. The average RNFL revealed a significant negative connection with age (P = 0.005). In glaucomatous eyes, the majority of researchers discovered significant correlation between CCT and RNFL.[6] Other researchers studied the correlation between the CCT and RNFL in normal individuals [7]. As, Henderson et al., Who studied the relationship between CCT and RNFL in normal individuals and POAG patients and reported that there was no association between the CCT and RNFL in healthy people or glaucomatous patients, which is consistent with the current study. [9]

Our results showed that the mean Total ganglion cell layer (GCL+) of the studied POAG patients was 59.63 ± 7.36. The mean superior ganglion cell layer (GCL+) of the studied POAG patients was 59.6 ± 7.54 while the mean inferior GCL+ of the studied POAG patients was 59.68 ± 8.016. The results showed that there was no significant correlation between CCT & total GCL+ (r= 0.037, p= 0.781). There was no significant correlation between CCT & superior GCL+ (r= 0.021, p= 0.876). Also, there was no significant correlation between CCT & inferior GCL+ (r= 0.056, p= 0.672) and as well, our results shows that there was significant negative correlation between corrected IOP and total GCL+ in the studied POAG patients (r= -0.521, p<0.001).

There was significant negative correlation between corrected IOP and superior GCL+ in the studied POAG patients (r= -0.446, p<0.001). Also, there was significant negative correlation between corrected

IOP and inferior GCL+ in the studied POAG patients (r= -0.534, p<0.001).

In agreement with our findings the study of Mahdy et al., reported that structural parameters including superior and inferior GCL thickness was significantly reduced in POAG groups compared to normal control, also there was a highly significant difference between Mild Vs Severe and Moderate Vs Severe Glaucoma groups as regard Superior and inferior GCL thickness, but there is no statistically significant difference between Mild Vs Moderate glaucoma groups as regard Superior and inferior GCL thickness. [10]

In contrast with our findings Al Saad et al., revealed that there is no statistically significant relationship was detected between CCT and RNFL or macular GCL+ thickness. That is not surprising considering their anatomical and physiological independence as they explain this finding in their study. [8]

The current result showed that there was significant negative correlation between corrected IOP and total RNFL in the studied POAG patients (r= -0.547, p<0.001). There was significant negative association between corrected IOP and superior RNFL in the studied POAG patients (r= -0.559, p<0.001), and there was significant negative association between corrected IOP and inferior RNFL in the studied POAG patients (r= -0.501, p<0.001).

However, Medeiros et al., in their observational cohort study they reported that there is no significant relationship between RNFL thickness at time of diagnosis and rate of RNFL loss (P = 0.69) when corrected for IOP. They also observed higher RNFL thickness with higher CCT (P <0.001), There is a 5.12 μm increase in RNFL thickness for Each 100 μm increase in corneal thickness. On the other hand, no significant association detected between CCT and RNFL loss over the study period serial measures (P = 0.064). When comparing RNFL thickness in glaucoma and glaucoma suspect eyes they found that glaucomatous eyes showed an average of 3.53 μm thinner RNFL than glaucoma suspect at time of diagnosis.[11]

The study of Kim et al., reported that higher preoperative peak IOP and IOP reduction were strongly associated with a larger decrease in mean RNFL thickness (p <0.001). On the other hand, postoperative mean IOP was not associated with postoperative loss of RNFL thickness (p = 0.451).[12]

CONCLUSION

From the data supported by the study, we found a positive association between CCT and inferior RNFL, but no significant association between CCT and IOP, macular GCL, Total RNFL, or superior RNFL thickness in the studied POAG cases. We also found significant negative associations between corrected IOP Versus total, superior and inferior GCL+ in the studied POAG patients. There were also significant negative associations between corrected IOP Vs. total, superior and inferior RNFL in the studied POAG patients. So, we recommend Further studies on large geographical scale and on larger sample size to emphasize our conclusion.

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