Macular thickness assessment in patients with primary open-angle glaucoma and its correlation with central visual field

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Background
Glaucoma is a multifactorial chronic optic neuropathy characterized by typical optic nerve morphological changes and alterations of the visual field (VF). Delayed detection and treatment of glaucoma might result in irreversible blindness. Structural damage precedes the functional damage.
Objective
The objective of this study was to correlate between macular thickness (MT) affection and central VF changes in patients with primary open-angle glaucoma (POAG).
Patients and methods
This is a prospective cross-sectional observational study that included 51 eyes diagnosed with POAG. They were evaluated by spectral domain optical coherence tomography, which was compared with several VF parameters, including mean deviation and loss variance.
Results
A significant correlation was found between VF parameters and decrease in MT (mean deviation: r=–0.506; P=0.000, loss variance: r=–0.492; P=0.000). There was also a significant correlation between thinning of the superior temporal and inferior temporal retinal nerve fiber layer and the decrease of the superior and inferior MT, correspondingly ($P<0.001$).
Conclusion
Measurements of the retinal thickness in the macula may be an additional tool for early detection of structural changes and its correlation with functional defects. Measuring the MT by spectral domain optical coherence tomography and using VF 10-2 degrees should be a standard technique in evaluation and follow-up of patients with primary open-angle glaucoma, although the VF is a time-consuming technique.

Keywords:
macula, primary open-angle glaucoma, optical coherence tomography, retinal nerve fiber layer, visual field

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Introduction

Glaucoma is one of the leading causes of blindness worldwide. It is a group of ocular diseases characterized by optic neuropathy associated with progressive thinning of the neuroretinal rim and loss of the retinal nerve fiber layer (RNFL) together with a particular pattern of visual field (VF) loss. Compared with standard automated perimetry, which is a functional and subjective test with greater intertest variability, optical coherence tomography (OCT) provides a highly qualitative, objective, and reproducible structural assessment of the optic nerve, RNFL, and macular thickness (MT) [1].

OCT has changed the ophthalmic care for patients with glaucoma, in particular, imaging of the optic nerve and circumpapillary RNFL [2]. Previous studies have reported that the correlation between peripapillary RNFL thickness measured by OCT and visual function is highly significant [3].

There is growing evidence that early glaucoma can affect the macula and cause paracentral VF deficits [4]. However, the routine VF test using the Humphrey field analyzer with the Swedish interactive threshold algorithm 24-2 or 30-2 programs has test points spaced 6° apart, with only four test points placed within the central 8° of the VF. Paracentral scotomas in certain patients can be overlooked in the routine 24-2 or 30-2 VF tests because of relatively poor central VF sampling [5]. In contrast, the 10-2 VF program has 68 test points within the central 10° and thus provides more detailed information in the central VF [5].

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This study aimed to correlate between MT and central VF affection in patients with primary open-angle glaucoma (POAG).

Patients and methods

This is a prospective cross-sectional observational study that was conducted on 51 eyes diagnosed with POAG. They were evaluated by spectral domain optical coherence tomography (SD-OCT), which was compared with several VF parameters: mean deviation (MD) and loss variance (LV). On the basis of the total macular thickness (TMT), which is the mean TMT of this study patients obtained by SD-OCT, the sample was divided into two groups:

(1) TMT < 278 μm (group A).
(2) TMT ≥278μm (group B).

The following was determined:

(1) Correlation between TMT and VF (analysis of two parameters in VF: MD and LV).
(2) Correlation between asymmetry in superior and inferior MT and LV.
(3) Correlation between superior versus inferior MT and the thinning of superotemporal and inferotemporal RNFL thickness, correspondingly.

All patients were fully informed about the procedure and signed a written informed consent to participate in the study. The protocol of this research was approved by the Research Ethics Committee of the Faculty of Medicine of Alzhar University.

Inclusion criteria

Male or female patients, age above 40 years, and previously diagnosed as POAG were the inclusion criteria.

Exclusion criteria

We excluded patients with secondary open-angle glaucoma, diabetic patients, hypertensive patients, patients with history of previous intraocular surgery, and patients with any other diseases that can affect the macula. We also excluded patients with poor-quality VF and OCT.

Spectral domain optical coherence tomography

The SD-OCT, SPECTRALIS (Heidelberg Engineering GmbH, Heidelberg, Germany) was used to study the macula and peripapillary area. It uses confocal laser scanning for image acquisition, by focusing the laser beam on the retina. Two different light beams are used simultaneously to obtain three-dimensional volume scans. These beams are deflected through oscillating mirrors, which allow a sequential scan of the retina and the creation of high-resolution spatial images with a scanning proximity of 11 μm. It is possible to compare the volume and thickness of the retinal layers, by comparing the values obtained from an individual with a normative database of normal individuals.

Macular assessment was conducted using the macular assessment protocol posterior pole '*p. pole*,' which encompasses a 30×25° scan with 61 scans per section. The default position was in the center, yielding 8×8 mm grid, and then TMT was evaluated with its superior and inferior subdivisions which is the mean retinal thickness for the superior and inferior hemispheres. TMT is the total mean thickness over the entire 8×8 mm grid centered on the foveal pit. All images obtained had a quality above 15 (above 20 considered best quality, above 15 considered medium quality, and from 10 considered low).

The RNFL thickness was analyzed for optic disc evaluation, using the glaucoma protocol for RNFL evaluation with a scanning pattern of 12° centered on the head of the optical disc. The default pattern position was 2.6° nasal and 2.1° superior from the fovea, and only one scanning per section was performed. The global thickness and six areas of the peripapillary region (temporal – T, inferotemporal – IT, inferonasal – IN, nasal – N, superonasal – SN, and superotemporal – ST) were analyzed using a STINT pattern.

Static computerized perimetry

VF analysis was done by 10-2 degree program, using Octopus 101 (Haag-Streit AG, Köniz, Switzerland). The basic parameters used were room with white lighting 1.27 or 10 cd/m^2, a white stimulus with a diameter of 0.43° (corresponding to the III size in Goldmann perimetry), and a time of exposure of 100 ms. Data were collected for statistical analysis parameters: MD and LV. MD measures the difference between the normal values, adjusted for the patient's age, and the sensitivity values of the patient. MD increase would reflect a sensitivity decrease, thus measuring diffuse VF changes in relation to what is considered normal. LV corresponds to the variance of the sensitivity determination thresholds, where increased LV indicates areas with different sensitivity thresholds, that is, focal or localized defects.

Statistical analysis

Data were collected, revised, coded, and entered to the statistical package for social science, version 23 (IBM Corp., Armonk, New York, USA). The quantitative data were presented as mean, SD, and range when their distribution found parametric and median with interquartile range. Spearman's correlation coefficients were used for statistical correlations. The *P* value was considered significant if less than 0.05.

Results

The mean age of the patients was 55.28±9.50 years (range: 40–77 years). POAG eyes included 27 right eyes (52.9%) and 24 left eyes (47.1%).

Twenty-four eyes were with TMT less than 278 µm (group A), with median age of the patients of 56.5 years and ranged from 44 to 77 years, including 10 right eyes (41.7%) and 14 left eyes (58.3%). Twenty-seven eyes were with TMT of at least 278 µm (group B), with a median age of the patients of 55 years, and range from 40 to 62 years, including 17 right eyes (63%) and 10 left eyes (37%).

The results obtained are summarized in Table 1.

The relation between TMT and age was nonsignificant (r=–0.111, P=0.565) as well as with macular asymmetry (MA) (r=–0.042, P=0.770). There was a statistically significant negative correlation between TMT and MD (r=–0.506, P=0.000) as well as between TMT and LV (r=–0.492, P=0.000, Table 2 and Figs 1 and 2).

Further assessment was done to get the relationship among TMT, MD, and LV within TMT less than 278 µm (group A) and TMT more than 278 µm (group B). In TMT less than 278 µm group, there was a significant correlation between TMT and MD as well as between TMT and LV (MD: r=–0.611, P=0.002 and LV: r=–0.410, P=0.047). When evaluating these parameters within patients with TMT more than 278 µm, there was a nonsignificant

Table 2 Correlation between total macular thickness and age, macular asymmetry, mean deviation, and loss variance

	Total thickness	
Parameters	*R*	*P* value
Age	–0.111	0.565
Macular asymmetry	–0.042	0.770
MD	–0.506**	0.000
LV	–0.492**	0.000

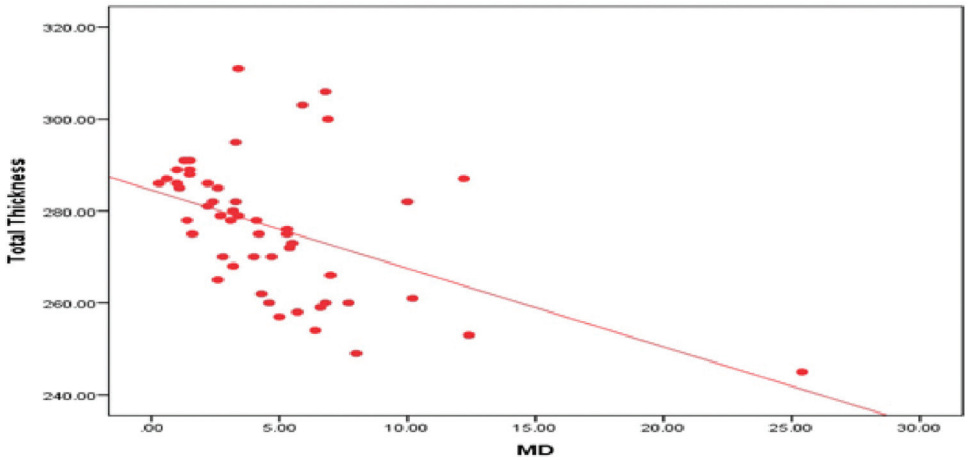
MD, mean deviation; LV, loss variance. **significant correlation.

Table 1 Median values obtained by optical coherence tomography and visual field in the subgroups

Parameters	Group A (*n*=24) Total thickness <278 µm	Group B (*n*=27) Total thickness ≥278 µm
Total Thickness		
Median (IQR)	263.5 (258.5–271.0)	286 (281.00–291.00)
Range	245–276	278–311
Superior		
Median (IQR)	265 (259.00–272.50)	283 (279.00–288.00)
Range	248–278	245–314
Inferior		
Median (IQR)	265.5 (256.5–270.0)	291 (284.00–295.00)
Range	243–288	276–319.00
Macular asymmetry		
Median (IQR)	5 (2.0–9.0)	6 (2.00–11.00)
Range	1–26	1–74
Superior temporal RNFLT		
Median (IQR)	94 (67.5–102.0)	110 (90.00–126.00)
Range	51–142	66–149
Inferior temporal RNFLT		
Median (IQR)	99 (74.5–112.0)	141 (114.00–155.00)
Range	48–141	61–175
MD		
Median (IQR)	5.35 (4.25–6.9)	2.60 (1.40–3.40)
Range	1.6–25.4	0.30–12.20
LV		
Median (IQR)	2.30 (1.80–4.55)	1.45 (1.30–2.10)
Range	1–7.50	1.10–7.40

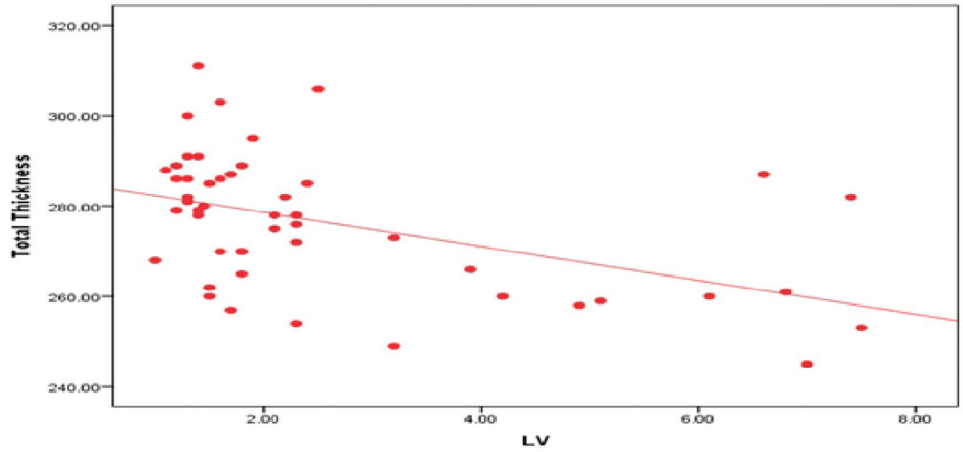
The asymmetry between superior and inferior macular thickness was calculated by subtracting the two corresponding values. IQR, interquartile range; LV, loss variance; MD, mean deviation; RNFLT, retinal nerve fiber layer thickness.

Figure 1



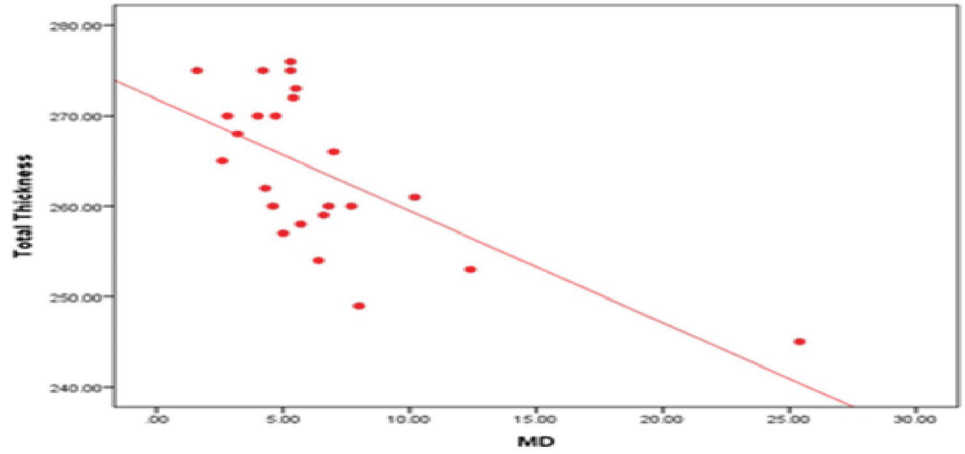
Correlation between total macular thickness and mean deviation (MD).

Figure 2



Correlation between total macular thickness and loss variance (LV).

Figure 3

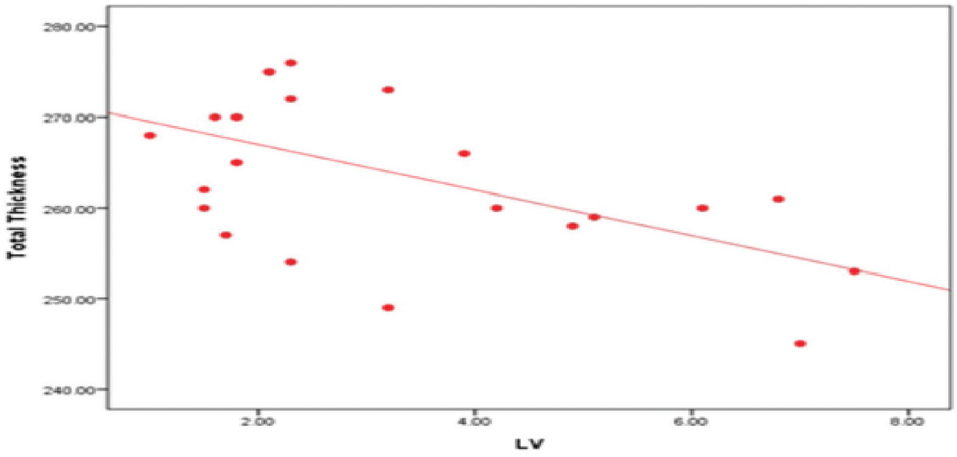


Correlation between total macular thickness less than 278 μm and mean deviation (MD).

correlation between TMT and MD as well as between TMT and LV (MD: r=0.052, P=0.796 and LV: r=−0.054, P=0.790, Figs 3 and 4).

We explored the relationship between asymmetry in the superior and inferior MT and the LV. We defined MA as the absolute value of the difference between

Figure 4



Correlation between total macular thickness less than 278 μm and loss variance (LV).

Table 3 Correlation between macular asymmetry and loss variance

	Macular asymmetry			
	Total thickness <278 μm		Total thickness ≥278 μm	
	R	*P* value	*R*	*P* value
Loss variance	0.037	0.863	0.285	0.150

superior and inferior MT. We did not find an overall significant correlation between MA and LV in both groups (A and B) (r=0.037, P=0.863 in group A and r=0.285, P=0.150 in group B, Table 3).

When comparing the superior MT with thinning of the superotemporal RNFL in both subgroups, a significant correlation was found as follows:

(1) TMT <278 μm (group A): r=0.648 and P=0.001.
(2) TMT >278 μm (group B): r=0.479 and P=0.012.

This indicates that as the superior MT decreases, so does the superotemporal RNFL thickness.

When comparing the inferior MT with thinning of the inferotemporal RNFL, only group A (TMT<278 μm) showed a significant correlation (r=0.570 and P=0.004), whereas group B (TMT>278 μm) showed nonsignificant correlation (r=0.135 and P=0.503). This indicates that as the inferior MT decreases, so does the inferotemporal RNFL thickness (Fig. 5).

Discussion

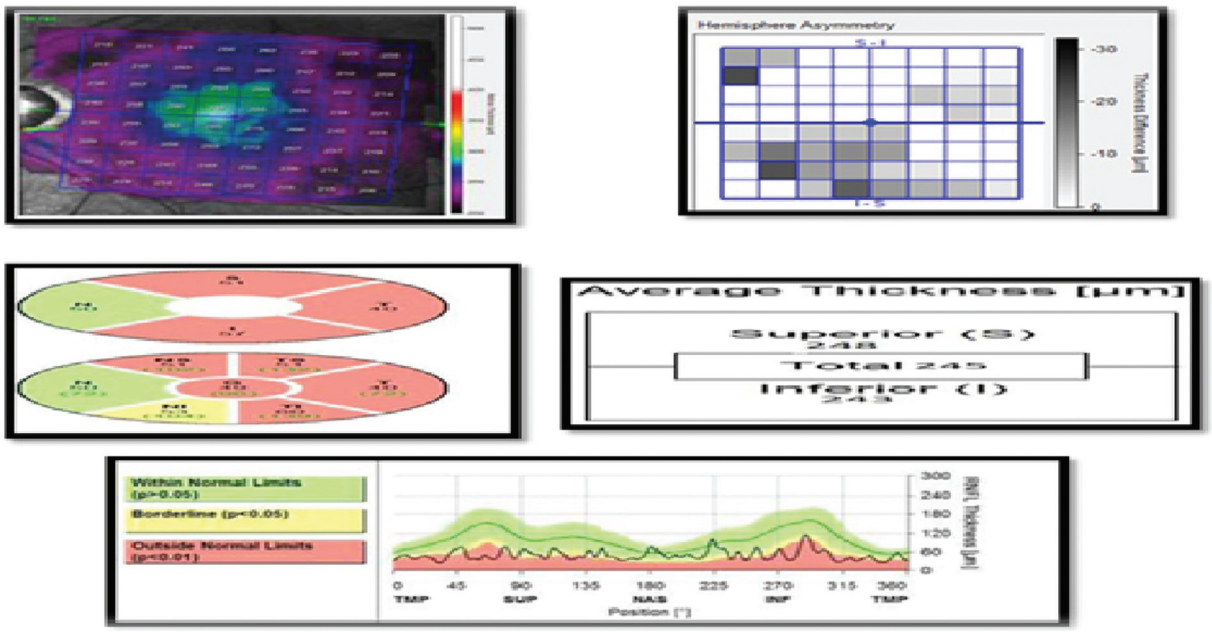
A largely overlooked study by Langerhorst *et al.* [6], prospectively obtained 10-2 (2° grid) and 30-2 (6° grid) VF data on 121 patients who were suspects or showed signs of early glaucoma. Defects were commonly seen on 10-2 ones, that is, within the central±10°. In addition, Schiefer *et al.* [7] reported that more than 50% of eyes with mild to moderate glaucoma had defects within the central±3°. Clearly, early glaucomatous VF damage often involves the central ±10°, and this damage can be underestimated, and even missed, with the 24-2 and 30-2 tests. By using the 10-2 test, we can achieve higher accuracy in defining the structure–function relationship. The 68 points within the central 10-2 degrees have provided more detailed information.

The present study showed a strong negative correlation between TMT and MD as well as between TMT and LV in group A (<278 μm). This disagrees with Mota *et al.* [8] who reported no correlation. When evaluating these parameters within group B (>278 μm), there was a nonsignificant correlation between TMT and MD, which agrees with Mota *et al.* [8]. However, there was a nonsignificant correlation between TMT and LV, which is in contrast with Mota *et al.* [8], who showed significant negative correlation between the TMT and LV in group B.

In glaucoma, particularly in earlier stages, there is localized cell loss, mainly in regions, such as the superotemporal and inferotemporal peripapillary quadrants. We found a moderate significant correlation between the decrease of the superior and inferior MT and thinning of the superotemporal and inferotemporal RNFL.

In the relationship between superotemporal RNFL and superior MT in both groups, there was a significant correlation in both groups, which is unlike the results of

Figure 5



Example showing the positive correlation between decreased macular thickness and thinning of superotemporal and inferotemporal quadrants. INF, inferior; N, nasal; NAS, nasal; NI, inferonasal; NS, superonasal; RNFL, retinal nerve fiber layer; SUP, superior; T, temporal; TI, inferotemporal; TMP, temporal; TS, superotemporal.

Mota *et al.* [8] which showed no significant correlation in both groups. However, in the relation between inferotemporal RNFL and inferior MT, there was a significant correlation in group A (TMT<278 µm), whereas no significant correlation in group B, which is in contrast with Mota *et al.* [8], who showed a significant relation in both groups. These results agree with some studies such as Hood *et al.* [9] and Park *et al.* [10], which claim that cellular damage in glaucoma is more severe in inferior macula. The results also suggest that axonal and ganglion cell loss occurs both in the macula and in the peripapillary region and that these changes seem correlated, denoting that RNFL and macula analysis are important parameters in early diagnosis of glaucoma.

By observing the asymmetry between the superior and inferior MT and LV, the results were nonsignificant in both groups A and B, which is in contrast with a study conducted by Mota *et al.* [8], which showed statistically significant results, suggesting that in patients with lower TMT, superior and inferior macular asymmetries correlate with focal defects present in the VF. Obtained results point toward macular asymmetries being better observed when the TMT is thinner, reflecting greater damage in the RNFL.

We have encountered some limitations associated with SD-OCT and 10-2 VF examinations while conducting our analyses. We minimized potential bias factors in the data obtained from SD-OCT through the acquisition of multiple images for each examination and the choice of images with overall good reliability standards. Another possible limitation of this study is that other diseases may cause visible structural changes, such as macular diseases. We dealt with this potential bias by excluding from this study all patients with other concomitant retinal pathologies.

Regarding the 10-2 VF, we excluded tests with low reliability and considered only patients who had already undergone two imaging, to minimize learning effect bias. VF defects (translated by an increased MD) may also be present in other diseases, such as cataract. To minimize this potential bias factor, we did not include in this study patients with significant eye media opacities. These tests are more time-consuming tests and may be difficult to perform owing to long time of examination for each eye.

In agreement with the aforementioned previous studies, we observed positive correlations between macular retinal thickness and central VF. The use of the 10-2 test for central VF testing is unique in the present study because it more accurately represents visual function in the macula. There is growing evidence that early glaucomatous damage involves the macula and causes corresponding central field change [4,9].

Conclusion

There were significant correlations between macular retinal thickness and central VF. The reduction of retinal thickness at the macular area was associated with the loss of the central VF in patients with early-stage and moderate-stage glaucoma. This relationship was demonstrated with 10-2 degree VF made with Octopus 101 and SD-OCT. SD-OCT measurements of retinal thickness in the macula correlate with RNFL parameters in patients with glaucoma. These results can be a valuable aid for evaluating and monitoring of patients with glaucoma, establishing a correlation between structure and function. Measurements of TMT in the macula may be an additional tool for early detection of structural changes and its correlation with functional defects.

Conflicts of interest

There are no conflicts of interest.

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