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Research Article

Correlation between Short-Wavelength Automated Perimetry and Retinal Nerve Fiber Layer Thickness Measured by Optical Coherence Tomography in Glaucomatous Eyes

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Abstract

Purpose: Evaluation of the topographic correlation between the retinal nerve fiber layer thinning (RNFL) measured by Optical Coherence Tomography (OCT) and decreased retinal sensitivity measured by short wavelength automated perimetry (SWAP) in glaucomatous patients.

Design: A prospective non- randomized cross sectional study.

Subjects and Methods: Thirty-five eyes from 35 patients with early glaucoma were selected from outpatient clinics in Mansoura Ophthalmic Center, Mansoura University, Egypt. This study included patients with primary open-angle, pseudoexfoliative and pigmentary glaucoma. Peripapillary RNFL thickness was measured using Spectral-Domain OCT. Visual field (VF) testing was done using SWAP. Visual field (VF) testing and OCT were performed within 6 weeks.

Main Outcome Measures: RNFL measurements were taken at 30° sectors (12 sectors described as clock hours). SWAP average pattern deviation (PD) (within 21 VF zones) was determined. The number of OCT-measured RNFL sectors (outside of normal limits) and the number of VF zones (outside of normal limits) were compared. Correlations between deviation from normal (thinner than 97.5% of normal) RNFL measurements and SWAP average PD were performed.

Results: OCT sectors 6 O'clock, 7 O'clock, 8 O'clock, 9 O'clock and 10 O'clock (inferior, infero- temporal and temporal) and SWAP VF zones 13, 14, 15, 16, 17 and 18 (superior hemifield central and arcuate areas) were most frequently damaged. In general, the strongest associations were detected between inferior and infero-temporal RNFL sectors (e.g. 6 O'clock, 7 O'clock) and superior nasal/arcuate VF zones (e.g. zones 13, 14, 15, 16, 17). Most non significant associations were found between superior RNFL sectors and superior VF zones.

Conclusion: There was topographic correlation between RNFL thinning measured by OCT and decreased retinal sensitivity measured by SWAP in early glaucoma patients. The combination of the structure-function methods can improve diagnosis of early glaucoma and help in prediction of glaucoma progression.

Keywords: Retinal nerve fiber layer thickness; Optical coherence tomography; Short wavelength automated perimetry and visual field

Introduction

The importance of evaluating retinal nerve fiber layer (RNFL) thickness to diagnose and monitor patients with glaucoma has been documented by several studies [1-3]. Recently, quantitative measurement of peripapillary RNFL thickness has been accurately done using different instruments. Spectral-domain Optical Coherence Tomography (OCT) is one of these techniques. It enhances the ability to diagnose glaucoma through objective, quantitative, and reproducible data [3,4]. OCT has been successfully used to detect RNFL defects in glaucomatous eyes with standard automated perimeter (SAP) defects [5]. Although SAP has poor sensitivity for detecting early loss of retinal ganglion cells [6], many studies showed that there is topographic relationship between SAP results and OCT in glaucomatous eyes [7].

Short–wavelength automated perimetry (SWAP) has greater sensitivity to early glaucoma than SAP. The SWAP detects glaucomatous defects earlier and more extensively than SAP because of its ability to measure a specific visual function associated with a

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subset of retinal ganglion cells [8].

The purpose of this study was to assess the topographic correlation between RNFL thinning and glaucomatous VF defects measured by SWAP. It was hypothesized that there is a topographic correspondence between OCT and SWAP measurements outside of normal limits. In addition, it was hypothesized that extent of the deviation from normal-value measurements using both instruments would be associated topographically.

Patients and Methods

The study design adhered to the tenets of the Declaration of Helsinki and was approved by the appropriate Institutional Review Board (IRB). Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Thirty-five eyes from 35 patients with early glaucoma were selected from outpatient clinics of Mansoura Ophthalmic Center, Mansoura University, Egypt. Subjects with primary open-angle glaucoma, normal-tension glaucoma, pseudoexfoliative glaucoma, and pigmentary glaucoma were included. When both eyes fulfilled the inclusion criteria, only one eye per subject was randomly selected.

The inclusion criteria included: best-corrected visual acuity ≥20/30 (Snellen), refractive error less than 5 spherical diopters and 2 diopters of cylinder, clear cornea, transparent ocular media (nuclear color/opalescence, cortical, or posterior subcapsular lens opacity <1) according to the Lens Opacities Classification System III system [9], C/D ratio (0.4-0.6), reproducible thinning of Peripapillary RNFL thickness in at least one 30° sector and open-anterior chamber angle. The exclusion criteria were as follows: previous intraocular surgery, diabetes or other systemic diseases, history of ocular or neurologic disease, ocular hypertensive individuals (intraocular pressure [IOP] higher than 20 mmHg and normal SAP).

All patients had a complete ophthalmological examination: clinical history, best-corrected visual acuity (BCVA), slit–lamp examination, gonioscopy, Goldmann applanation tonometry, fundus examination including Cup Disc ratio. Peripapillary RNFL thickness was measured using Spectral-Domain OCT. Visual field (VF) testing (central 24-2) was performed using SWAP. Patients with low test reliability were excluded from the study. The full ophthalmic examination, VF testing, and OCT were performed within 6 weeks of the subject's date of enrolment into the study

The mean [±standard deviation (SD)] age of these patients was 43.05 ± 8.62 years. Nineteen (54.3%) were females, and sixteen (45.7) were males.

Instrumentation

Optical coherence tomography (OCT)

Topcon 3D-OCT 1000 using new detection techniques known as spectral / fourier domain detection which can dramatically improve the sensitivity and imaging speed of OCT [10]. Fourier domain detection techniques measure the echo time delay of light by measuring the spectrum of the interference between light from tissue and light from a stationary un-scanned reference arm. Fourier detection uses a spectrometer a high–speed charge coupled device line scan camera to measure the interference spectrum. The echo time delays of the back scattered or back-reflected light from the tissue can be measured by taking the fourier transform of the interference spectrum, hence the name fourier domain detection [11]. The reported RNFL thickness measurements were determined by the mean of the 3 images obtained.

The reported OCT summary data represent the RNFL thickness measured in 12 hours each 30° sectors, with 12-o´clock in the superior position and 9-o´clock in the temporal position.

Comparison between the values of the nerve fiber thickness at each sector in each eye and an age–matched normative database of subjects was done. Calculation of deviation from normal values was performed. Sectors with RNFL thickness thinner than 97.5% of the normals were considered outside of normal limits [12].

Short–wavelength automated perimetry (SWAP)

It is a modification of SAP using the perimeter and programs. It uses a 440 nm, 1.8° target at 200 milliseconds' duration on a 100 candelas / m^2 yellow background to test selectively the short wave length sensitive cones and their connections [13]. The test is most likely carried out by the small bistratified blue–yellow ganglion cells, which constitute approximately 9% of the total population of retinal ganglion cells [14].

Study eyes had ≥ 2 consecutive abnormal SWAP results (glaucoma hemifield test results outside of normal limits or corrected pattern standard deviation [CPSD] outside of 95% limits). There was reproducible location of localized VF defects. VF testing was unaffected by any testing artifacts, for all participants. Previous many studies show that SWAP abnormalities have more reproducibility than SAP abnormalities [9].

Mapping OCT to SWAP

To map OCT results to SWAP results. The number of eyes with OCT clock hour thickness measurements outside normal limits was determined as previously mentioned. For topographic analysis, the SWAP VF was divided into 21 zones [7,15], to detect the correlation between each zone and each RNFL sector. The number of abnormal VF zones (outside of normal limits) was recognized as follows: if a zone composed of 1 or 2 test points included 1 individual test point with a Pattern Deviation (PD) outside of normal limits (P≤ 5%), or if a zone composed of ≥ 3 test points included ≥ 2 test points with PD outside of normal limits.

The topographic association between quantitative data from OCT and VF loss detected with SWAP depended on the frequency of simultaneous VF and RNFL damage for each patient, the topographic comparison for OCT and SWAP for glaucomatous defects was transferred to a damage information table. This table was a 12×21 matrix with 12 columns (OCT sectors 1-o'clock --- 12-o'clock) and 21rows (SWAP VF zones 1-21). The number 1 was assigned to the corresponding cell when the eye had a defect at both the corresponding sector and the zone; otherwise the number 0 was assigned. A frequency summary table was established by summing all 35 patients' damage information tables. Also, linear regression analysis (Pearson's correlation coefficient) (R2) was done to assess the correlation between the average deviation from mean normal RNFL thickness (measured in microns) in each sector (1-o'clock ---

Table 1: Frequency of OCT defect, average thickness (μm), and deviation from normal (μm) for each clock hour RNFL sector for all eyes (n=35).

	The Number of Eyes with Defect (%)	Average RNFL Thickness (±SD) (μm)	Average Normal RNFL Thickness (±SD) (μm)	Deviation from Normal (μm)
1-O'clock	7 (20)	70.00 (11.54)	109.87 (14.28)	-39.87
2- O'clock	8 (22)	53.50 (6.14)	85.87 (13.64)	-32.37
3- O'clock	11 (31)	36.90 (7.95)	64.13 (11.70)	-27.23
4- O'clock	7 (20)	44.71 (4.02)	79.80 (13.37)	-35.09
5- O'clock	9 (25)	65.11 (16.82)	99.12 (14.04)	-34.01
6- O'clock	13 (37)	78.84 (18.80)	123.86 (14.03)	-45.02
7- O'clock	17 (48)	80.29 (13.08)	119.09 (17.20)	-38.90
8- O'clock	13 (37)	44.23 (6.01)	66.48 (12.12)	-22.25
9- O'clock	16 (45)	35.25 (7.93)	57.50 (8.77)	-22.25
10-O'clock	13 (37)	52.76 (7.02)	80.86 (11.76)	-28.10
11- O'clock	12 (34)	84.33 (1028)	114.59 (13.78)	-30.26
12- O'clock	11 (31)	78.63 (6.81)	116.50 (18.67)	-37.87

SD: Standard Deviation

Table 2: Frequency of SWAP visual field defect and mean pattern deviation (Decibels) for all visual field zones for all eyes (n=35).

Visual Field Zone	The Number of Eyes with Defect (%)	Mean Pattern Deviation (±SD)
1	0 (0)	-
2	0 (0)	-
3	0 (0)	-
4	1 (2)	-3.08 (0.19)
5	3 (8)	-3.02 (0.49)
6	0 (0)	-
7	3 (8)	-2.59 (0.55)
8	4 (11)	-2.86 (0.19)
9	0 (0)	-
10	0 (0)	-
11	blind spot	blind spot
12	2 (5)	-2.045 (0.22)
13	10 (28)	-2.040 (0.48)
14	12 (34)	-2.67 (0.92)
15	9 (25)	-2.83 (0.99)
16	14 (40)	-2.96 (0.92)
17	19 (54)	-2.86 (0.83)
18	4 (11)	-2.79 (0.74)
19	4 (11)	-3.04 (0.51)
20	0 (0)	-
21	0 (0)	-

SD: Standard Deviation

12-o'clock and the average SWAP PD in each VF zone (1 – 21) except VF zone (11) corresponding to blind spot which was excluded. For all analysis, $P < 0.05$ was considered statistically significant.

Results

OCT - measured nerve fiber layer thickness was outside of normal limits in 1clock hour sector only in 9 (25%) eyes and outside of normal limits in at least 2clock hour sectors in 26 (75%) eyes. The frequency of OCT defects' average thickness (microns), deviation from normal (microns) for all clock hour positions for all eyes is shown in Table 1.

The 5 most frequently damage OCT sectors were 7-o'clock [17 eyes (48%)], 9- o'clock [16 eyes (45%)], 6-o'clock [13 eyes (37%)], 8-o'clock [13 eyes (37%)], and 10-o'clock [13 eyes (37%)]. The frequency of SWAP defects and mean PD values for each VF zone is shown in Table 2. The 5 VF zones most frequently outside normal limits were zones 17 [19 eyes (54%)], 16 [14 eyes (40%)], 14 [12 eyes (34%)], 13 [10 eyes (28%)] and 15 [9 eyes (25%)]. The most deviant mean PD values (± SD) were zones 4 (3.08 ± 0.19dB), 19 (3.04 ± 0.51dB) and 5 (3.02 ± 0.59dB).

Table 3 shows the frequency of RNFL clock hour damaged sectors for OCT and corresponding SWAP abnormal VF zones. Visual field defects in the superior hemifield zone tended to correspond most frequently with inferior RNFL damage as measured with OCT. RNFL thickness at 6-o'clock and 7-o'clock (inferotemporal) tended to correspond most frequently with VF zones 13, 14 and 16 (superior nasal step, central and superior arcuate) Figure 1.

The global correlations between SWAP (MD and CPSD) and OCT mean RNFL thickness were R^2 = 10% (P=0.057) and R^2 =1% (P=0.64) respectively. OCT clock hour position 6-o'clock and 7-o'clock (inferotemporal) had the strongest association with SWAP VF zone 14 (superior nasal region) R^2 = 76% (P=0.011) and R^2 =48% (P=0.012) respectively. OCT clock hour position 8-o'clock had the strongest association with SWAP VF zone 15 R^2 = 64% (P = 0.010).

In a very small number of cases, relatively strong structure function association was observed where they were not predicted. For instance, superior temporal OCT 10-o'clock and 11-o'clock was associated with SWAP VF zone 17 (P=0.028, and P= 0.005 respectively). Also, OCT 11-o'clock was associated with superior temporal SWAP VF zone 18 (P=0.018).

Discussion

The results of this study show a topographical correlation between OCT and SWAP measurements. These results document the relationship between regional OCT measured RNFL thinning in glaucoma patients and decreases in visual field zone sensitivity

Table 3: Frequency of defect summary table for 35 patients. The top row corresponds to OCT sectors while the left row corresponds to SWAP visual field zones.

Hours/Zones	1	2	3	4	5	6	7	8	9	10	11	12 CL
1												
2												
3												
4	1								1	1	1	
5	2			2					1	1	1	
6												
7	2	1	1	2						1	1	1
8	1									2	2	1
9												
10			1	1		1	2	1	1	2	3	2
11												
12									1	1	1	1
13	1				2	4	4	3	1	1	1	1
14		2	3	1	1	3	10	4	3	2	1	2
15					2	6	7	4	1	2	2	
16		1	1		3	7	10	5	1	2	2	
17		1	1		3	10	14	7	1	2	2	
18	1		1		2	3	4	1	1	3	2	1
19	1				1	2	1					2
20												
21												

in both location and severity [16]. In addition, these results confirm that SWAP is a valuable indicator of visual function of RNFL health. OCT–measured inferotemporal RNFL thinning (sectors 6-o'clock, 7-o'clock, and 8-o'clock) corresponded with SWAP damage in the superior nasal step / superior arcuate regions.

This study included eyes with mostly mild to moderate glaucoma. The average SWAP mean deviation (MD) was – 6.79 ± 2.17 decibels (dB) (range–3.67to–12.56). The average corrected pattern standard deviation (CPSD) was 2.17 ± 0.65 dB (range 0.79 to 4.12).

The global correlations between OCT mean RNFL thickness and SWAP global parameters (MD and CPSD) were R^2 = 10% (P=0.057) and R^2 =1% (P=0.64) respectively. While the regional associations between measured OCT RNFL thinning and SWAP PD was between 6-o'clock and 7-o'clock (inferior) and SWAP VF zone 14 (superior nasal region) was R^2 = 76% (P=0.011) and R^2 = 48% (P=0.012) respectively. Therefore, regional associations between RNFL thickness measurements and SWAP PD were stronger than global associations.

Quigley et al documented that there may be diffuse loss of up to 50% of axons without a localized VF defect on Goldmann manual perimetry using histopathologic studies [17]. Later on, they evaluated the relationship between histological findings of retinal ganglion cell atrophy and perimetry in 6 human glaucomatous eyes and estimated that 20% cell loss corresponded to locations with a 5 – dB sensitivity loss, and 40% cell loss correlated to a 10 – dB decrease in sensitivity [18].

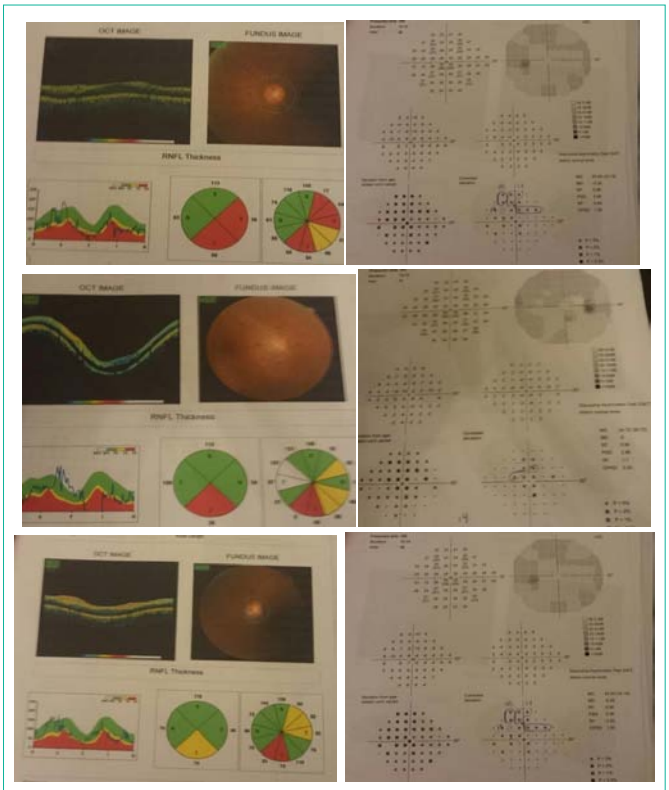

Figure 1: The correlation between sectorial RNFL thinning and SWAP test.

In this study, a quantitative method for RNFL analysis (OCT) was used. It was found that average deviations from normal RNFL thickness were 36% and 32% for 6- o'clock and 7-o'clock respectively. They were associated with average SWAP superior VF zones with PD values in the range of – 2.40 to – 2.86 dB. These findings were different from those of Quigley et al. [18], because SWAP–sensitive retinal ganglion cells represent only a small subset of total retinal ganglion cells. Zangwill et al. [19] used quantitative techniques. In their study there was a significant association between SAP MD both OCT RNFL thickness (R^2 =0.35 – 0.43) and RNFL photography evaluation (R^2 = 0.18 – 0.29) [19]. Correlations also have been documented between OCT-measured RNFL thickness and SAP global parameters (MD and CPSD) of between approximately R= 0.50 and R= 0.70 [20].

The results of this study were comparable to those from studies investigating the focal relationship between structure and function defects in glaucoma. In Abadia, et al. study, the glaucoma group showed mild to moderate correlations between the RNFL thickness measured with Cirrus OCT and the retinal sensitivity evaluated with SAP. The strongest correlations were found between the RNFL thickness at inferior quadrant and the superior hemifield points. The inferior RNFL thickness showed the greatest thinning (5, 6, and 7 clock-hour positions) and the strongest associations with the superior hemifield in glaucoma patients. Point 8 of HFA (anatomically corresponded with the retinal sensitivity of the arcuate nerve fiber bundle) and inferior quadrant thickness exhibited the strongest correlation (r = 0.534; P < 0.001) [21]. These results were consistent with prior studies and clinical findings, which have been trying to establish the relationship between SAP and OCT [22-26].

Anton et al. evaluated SAP and confocal scanning laser ophthalmoscope in patients with focal glaucomatous damage, finding inferior rim damage in 22 (84%) of 26 glaucomatous eye [27]. In this study, I found up to 48% of eyes with topographically correlating OCT and SWAP defects.

El Beltagi et al. [7] using SAP found that OCT measured RNFL thickness was most frequently abnormal in the inferior sector 6-O'clock and inferotemporal sectors 7-o'clock and 8-o'clock. The most frequently abnormal SAP VF zones were superior hemifield zones (14-16). Best correlation was detected between deviation from normal RNFL thickness at OCT clock hour position 6, 7 and 8 and SAP PD in the superior arcuate and nasal step regions (R^2 = 33% - 57%). The most affected sectors were 6- o'clock, 7 o'clock, and 8 o'clock. Using SWAP, I had similar results. The most frequently damaged SWAP zones by PD were 14 and 15 and regression results between inferior OCT sectors and superior SWAP VF zones were R^2 = 76% (P=0.011) and R^2 =48% (P=0.012) respectively.

Polo et al., investigated the relationships between morphologic changes of the RNFL using red-free photography, and SWAP defects in 160 eyes of 83 ocular hypertensive. SWAP results were abnormal in 35.6% (57 eyes), and the greater percentage of abnormal perimetric results was obtained in eyes with pathologic RNFL [28]. In another study, an increase in diffuse RNFL damage was associated with a decrease in SWAP MD in 49 ocular hypertensive eyes [29].

Also, Yamagishi et al investigated the relationship between focal VF zone damage (measured with SWAP) and focal rim damage (measured with confocal scanning laser ophthalmoscope) using the same VF zones in this study and demonstrated a correlation of VF defects and inferior rim damage in 11 (78%) of 14 glaucomatous eyes [30].

Conclusion

OCT measurement of RNFL thickness and SWAP measurement of visual function are topographically correlated in glaucoma. The combination of the structure-function methods can improve diagnosis of early glaucoma and help in prediction of glaucoma progression.

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