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Relationship between automated perimetry and Heidelberg retina tomograph, optic coherence tomography and laser polarimetry in moderate to severe glaucomatous eyes

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ABSTRACT

Objectives: To determine the correlations between the measurements obtained with Heidelberg retina tomograph III (HRT III), optic coherence tomography (OCT), and laser polarimetry (GDx) with the indices of automated perimetry (AP) in moderate and severe glaucoma patients.

Methods: Forty-nine eyes of 30 patients were included in the current study and were divided into two groups: 23 eyes with moderate and 26 eyes with severe glaucoma defined by Hodapp-Parrish-Anderson grading system. Pearson's correlation coefficients were used to evaluate the correlation between the indices of AP including mean deviation (MD) and pattern standard deviation (PSD), and structural parameters of the retinal nerve fiber layer (RNFL) and optic disc acquired by using three devices in both groups.

Results: In moderate glaucoma OCT and GDx measurements were not correlated to MD only the exception of inferior RNFL (r = 0.57, p = 0.007 and r = 0.52, p = 0.008, respectively). Mild to moderate correlations were calculated between the structural parameters of HRT III and AP indices. In severe glaucoma, the most correlated measurements were obtained by OCT compared to the other devices. The correlations for MD were more powerful compared to PSD. Parameters based on the study of the RNFL showed stronger correlations than those of the optic nerve head. No devices showed significant correlations in patients with MD less than -12 dB.

Conclusions: OCT measurements showed the best correlations with the AP indices in both moderate and severe glaucoma patients. However, AP still seems to be more effective in the follow-up of glaucoma progression in more advanced glaucomatous damage.

Keywords: automated perimetry, Heidelberg retina tomograph, laser polarimetry, optic coherence tomography, glaucoma

Glaucoma is an optic neuropathy associated with the loss of retinal ganglion cells and their axons which create the retinal nerve fiber layer (RNFL) [1]. Several studies have shown that morphological

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changes of optic disc and defects in visual field (VF) are valuable indicators for diagnosis of glaucoma.

Although automated perimetry (AP) is the gold standard method for glaucoma diagnosis and progression documentation, morphological changes of optic disk and RNFL may precede VF defects in some cases [2]. Several studies have shown the efficacy of Heidelberg Retina Tomograph laser scan (HRT), laser polarimetry (GDx) and optic coherence tomography (OCT) for detecting glaucomatous changes of optic nerve and RNFL [3, 4].

Automated perimetry is useful to determine cases with moderate and advance glaucoma however it may be insufficient to detect patients in early stages [5, 6]. In the other hand the recently imaging techniques have been reported to detect early stages of glaucoma [7]. In this study, we aimed to evaluate the structural parameters of the optic nerve head and RNFL obtained by using a HRT III, OCT and GDx with global indices of conventional AP and reveal the diagnostic precision of these devices for detecting and following subjects with moderate and severe primary open angle glaucoma (POAG).

METHODS

Patients

In this prospective study 49 eyes of 30 patients with POAG were included and were classified into two groups: 23 with moderate and 26 with severe glaucoma. Exclusion criteria were the presence of corneal opacity or cataract, refractive errors higher than -7.0 to +4.0 Diopters (D) sphere and/or 3.0 D cylinder, visual acuity less than 20/100. The study was conducted in accordance with the ethical standards stated in the 1964 Declaration of Helsinki and approved by the Local Ethics Committee of the participating center. All patients were informed about the purpose of the study and provided their consent.

The definition of glaucoma was made by the findings of VF defects. The severity of the VF defect was graded as moderate, or severe visual field loss as defined by Hodapp-Parrish-Anderson (HPA) grading system criteria [8]. In this staging system, glaucomatous eyes were classified into three groups according to the mean deviation (MD) values (mild, MD < -6 dB; moderate, MD > -6 dB and < -12 dB; severe, MD > -12 dB).

A complete ophthalmic examination and also measurements of AP, HRT III, OCT and GDx were obtained in all patients.

Conventional Automatic Perimetry

In all patients 30-2 central field test which uses the Swedish Interactive Threshold Algorithm (SITA) standard software program version 24-2 (Carl Zeiss Meditec, Oberkochen, Germany) on a Humphrey 750i automatic visual field analyzer (Carl Zeiss Meditec) was performed [9]. The test object was size III; the duration time was 200 ms; and the background brightness was 31.5 asb (10 cd/m^2). Refractive errors and presbyopia were corrected before the examination. The test was accepted to be confidential when fixation loss, false-negative and false-positive rates were less than 30%. Abnormality was evaluated using the instrument's software through calculating the global Indices of MD or pattern standard deviation (PSD).

Confocal Scanning Laser Ophthalmoscope Imaging

Confocal scanning laser ophthalmoscopy measurements were obtained with the HRT III (Heidelberg Engineering) as described previously [10]. The same examiner performed 3 sequential measurements and these were aligned to combine unique image. The margins of the optic disc were marked by the same examiner manually. Once the margins were marked, disc parameters were estimated automatically by the device. The evaluated parameters in our study were rim area, rim volume, linear cup to-disk ratio, cup-to-disk area ratio, rim-to-disk area ratio, RNFL cross-sectional area, mean RNFL thickness, cup area, cup volume, and mean cup depth.

Optical Coherence Tomography

One examiner performed the peripapillary RNFL thickness measurements by the Stratus TD OCT (Carl Zeiss Meditec) which were described previously [11]. The accepted images had at least 7 signal quality. Study protocols were carried out for RNFL thicknesses (mean, superior and inferior), central foveal thickness and total foveal volume.

Laser Polarimetry

Scanning Laser polarimetry measurements were

obtained by using GDx VCC (Carl Zeiss Meditec Inc.). Details of the GDx-VCC operation have been described [12]. The device calculated the RNFL thicknesses for temporal, superior, nasal and inferior quadrants and nerve fiber indicator (NFI). Measurements with quality score grading less than 7 and scan score less than 70 were excluded.

Statistical Analysis

Statistical analyses were calculated using SPSS software (version 21.0, SPSS, Inc. Chicago, IL, USA). Kolmogorov–Smirnov test revealed that the data was normally distributed ($p > 0.05$). The results are presented as the mean ± the standard deviation (SD). The measurements between each group were compared by Paired t test. Correlation of measured parameters obtained by OCT, HRT III and GDx VCC with MD and PSD was analyzed with Pearson correlation coefficient. *P* value < 0.05 was considered statistically significant.

RESULTS

A total of 49 eyes of 30 patients (20 males, 10 females) with POAG were evaluated. The mean age of the patients was 56.2 ± 10.0 years. As defined by HPA grading system 14 patients (23 eyes) had moderate

Table 1. Comparison of the measured parameters obtained by OCT, HRT III and GDx between the groups

	Moderate POAG (n = 23)	Severe POAG (n = 26)	*p* value
OCT parameters			
RNFL superior (µm)	86.76 ± 17.74	57.80 ± 15.45	**0.001**
RNFL inferior (µm)	75.42 ± 16.32	54.76 ± 14.12	**0.001**
RNFL average (µm)	65.81 ± 7.88	51.72 ± 9.08	**0.001**
CFT (µm)	209 ± 24	175 ± 16	**0.001**
Total macular volume (µm)	5.83 ± 0.43	6.38 ± 0.37	**0.001**
GDx parameters			
TSNIT average (µm)	45.08 ± 2.50	38.40 ± 5.44	**0.001**
RNFL superior (µm)	52.38 ± 4.80	39.35 ± 8.26	**0.001**
RNFL inferior (µm)	51.21 ± 7.16	41.76 ± 9.17	**0.001**
NFI	47.04 ± 10.45	74.48 ± 15.94	**0.001**
HRT III parameters			
Cup area (mm^2)	1.03 ± 0.40	1.34 ± 0.42	**0.017**
Rim area (mm^2)	0.96 ± 0.30	0.76 ± 0.21	**0.026**
Rim volume (mm^3)	0.17 ± 0.07	0.14 ± 0.07	0.057
Cup/Discarea	0.53 ± 0.17	0.63 ± 0.13	**0.027**
Cup/Discarea (linear)	0.70 ± 0.12	0.79 ± 0.09	**0.010**
Average cup depth (mm)	0.27 ± 0.08	0.37 ± 0.15	**0.009**
Maximum cupdepth (mm)	0.57 ± 0.14	0.76 ± 0.26	**0.003**
Cup shape measure	-0.060 ± 0.002	-0.020 ± 0.001	**0.041**
RNFL average (µm)	0.14 ± 0.05	0.10 ± 0.07	**0.027**

Values are given as mean ± standard deviation. POAG = Primary open angle glaucoma, OCT = Optical coherence tomography, HRT = Heidelberg retina tomograph, GDx = Laser polarimetry, RNFL = Retinal nerve fiber layer, CFT = Central foveal thickness, TSNIT = Temporal-superior-nasal-inferior-temporal, NFI = Nerve fiber indicator. $p < 0.05$ indicates statistically significance difference.

POAG, 16 patients (26 eyes) had severe POAG. There were no significant differences in age and sex among the two groups ($p = 0.31$ and $p = 0.28$, respectively). Comparison of the measured parameters obtained by OCT, HRT III and GDx between the groups are shown in Table 1. All the measured parameters among the two groups were significantly higher for OCT and GDx ($p < 0.001$) and statistically significant for HRT III ($p < 0.05$).

Any correlations between the measured parameters and the AP indices of the moderate glaucoma patients are shown in Table 2. OCT and GDx measurements were not correlated to MD only the exception of inferior RNFL for both devices (r = 0.57, $p = 0.007$ and r = 0.52, $p = 0.008$, respectively). In addition there was no significant correlation between these devices and PSD. Regarding the measurements of HRT III, significant correlations were found between cup area, cup/disc area, cup/disc area (linear) and maximum cup depth and MD (r = -0.50, $p = 0.02$, r = -0.41, $p = 0.04$; r = -0.44, $p = 0.03$; r = -0.43, $p = 0.05$, respectively). Additionally, cup area, cup/disc area, cup/disc area (linear) and average RNFL were significantly correlated to PSD (r = -0.59, $p = 0.005$, r = -0.54, $p = 0.01$, r = -0.50, $p = 0.02$; r = 0.45, $p = 0.04$, respectively).

Correlations between the measured parameters and the AP indices of the severe glaucoma patients are

Table 2. Correlations between the measured parameters and the MD-PSD of the moderate POAG

	MD (n = 23)		PSD (n = 23)	
	r	*p* value	r	*p* value
OCT parameters				
RNFL average (µm)	0.20	0.38	-0.07	0.75
RNFL superior (µm)	0.10	0.67	-0.05	0.81
RNFL inferior (µm)	0.57	0.007	-0.05	0.83
CFT (µm)	0.43	0.051	-0.19	0.41
Total macular volume (µm)	0.20	0.41	0.05	0.84
GDx parameters				
TSNIT average (µm)	0.22	0.36	0.21	0.35
RNFL superior (µm)	0.18	0.45	-0.16	0.49
RNFL inferior (µm)	0.52	0.008	0.20	0.39
NFI	-0.14	0.54	0.06	0.78
HRT III parameters				
Cup area (mm^2)	-0.50	0.02	-0.59	0.005
Rim area (mm^2)	0.27	0.23	0.04	0.86
Rim volume (mm^3)	0.27	0.23	0.15	0.50
Cup/Disc area	-0.41	0.04	-0.54	0.01
Cup/Disc area (linear)	-0.44	0.03	-0.50	0.02
Average cup depth (mm)	-0.34	0.12	-0.30	0.18
Maximum cup depth (mm)	-0.43	0.05	-0.16	0.49
Cup shape measure	-0.03	0.88	-0.35	0.12
RNFL average (µm)	-0.06	0.79	0.45	0.04

POAG = Primary open angle glaucoma, OCT = Optical coherence tomography, HRT = Heidelberg retina tomograph, GDx = Laser polarimetry, RNFL = Retinal nerve fiber layer, CFT = Central foveal thickness, TSNIT = Temporal-superior-nasal-inferior-temporal, NFI = Nerve fiber indicator, MD =median deviation, PSD = pattern standard deviation. $p < 0.05$ indicates statistically significance difference.

shown in Table 3. The RNFL (average, superior and inferior) as measured by OCT was significantly correlated with MD (r = 0.74, p = 0.001; r = 0.68, p = 0.001; r = 0.70, p = 0.001, respectively). However, no significant correlation was found between OCT measurements and PSD (p > 0.05). The inferior RNFL and NFI obtained by GDx were significantly correlated with MD (r = 0.66, p = 0.001; r = -0.66, p = 0.001, respectively). Similarly no significant correlation was found between GDx measurements and PSD (p > 0.05). Regarding the measurements of HRT III, significant correlations were found between cup area, cup/disc area, cup/disc area (linear), average and maximum cup depth and cup shape measure and MD (r = -0.51, p = 0.01; r = -0.45, p = 0.03; r = -0.44, p = 0.03; r = -0.57, p = 0.003; r = -0.61, p = 0.001, respectively). Additionally, cup area and rim volume were significantly correlated to PSD (r = -0.54, p = 0.005; r = -0.47, p = 0.02, respectively).

In patients with MD less than -20 dB (12 patients), the measurements of OCT, GDx and HRT III did not show any significant correlation with MD and PSD (p > 0.05) (Table 4).

DISCUSSION

In this study we compared the structural parame-

Table 3. Correlations between the measured parameters and the MD-PSD of the severe POAG

	MD (n = 26)		PSD (n = 26)	
	r	*p* value	r	*p* value
OCT parameters				
RNFL average (µm)	0.74	**0.001**	0.16	0.45
RNFL superior (µm)	0.68	**0.001**	0.18	0.40
RNFL inferior (µm)	0.70	**0.001**	0.19	0.36
CFT (µm)	0.35	0.08	0.08	0.71
Total macular volume (µm)	0.33	0.11	0.14	0.50
GDx parameters				
TSNIT average (µm)	0.43	**0.045**	0.04	0.85
RNFL superior (µm)	0.47	**0.032**	-0.13	0.53
RNFL inferior (µm)	0.66	**0.001**	0.40	0.05
NFI	-0.66	**0.001**	-0.07	0.74
HRT III parameters				
Cup area (mm^2)	-0.51	**0.01**	-0.54	0.005
Rim area (mm^2)	0.34	0.09	0.04	0.79
Rim volume (mm^3)	0.20	0.34	0.47	0.02
Cup/Disc area	-0.45	0.03	-0.28	0.35
Cup/Disc area (linear)	-0.44	0.03	-0.35	0.06
Average cup depth (mm)	-0.57	0.003	-0.26	0.06
Maximum cup depth (mm)	-0.41	0.035	-0.34	0.06
Cup shape measure	-0.61	0.001	-0.38	0.06
RNFL average (µm)	-0.01	0.96	0.156	0.46

POAG = Primary open angle glaucoma, OCT = Optical coherence tomography, HRT = Heidelberg retina tomograph, GDx = Laser polarimetry, RNFL = Retinal nerve fiber layer, CFT = Central foveal thickness, TSNIT = Temporal-superior-nasal-inferior-temporal, NFI = Nerve fiber indicator, MD =median deviation, PSD = pattern standard deviation. p < 0.05 indicates statistically significance difference.

Table 4. Correlations between the measured parameters and the MD-PSD of the patients with MD less than -20 dB

	MD (n = 12)		PSD (n = 12)	
	r	*p* value	r	*p* value
OCT parameters				
RNFL average (µm)	0.50	0.12	-0.23	0.95
RNFL superior (µm)	0.42	0.20	0.32	0.34
RNFL inferior (µm)	0.50	0.12	-0.42	0.90
CFT (µm)	0.36	0.28	0.33	0.32
Total macular volume (µm)	0.35	0.62	0.01	0.96
GDx parameters				
TSNIT average (µm)	-0.53	0.09	-0.60	0.05
RNFL superior (µm)	-0.40	0.22	-0.43	0.06
RNFL inferior (µm)	-0.17	0.61	-0.23	0.37
NFI	0.20	0.55	0.47	0.05
HRT III parameters				
Cup area (mm^2)	-0.30	0.38	-0.38	0.22
Rim area (mm^2)	0.09	0.77	0.20	0.51
Rim volume (mm^3)	0.19	0.57	0.14	0.63
Cup/Disc area	-0.21	0.53	-0.22	0.42
Cup/Disc area (linear)	-0.24	0.47	-0.29	0.46
Average cup depth (mm)	-0.23	0.50	-0.35	0.51
Maximum cup depth (mm)	-0.11	0.75	-0.49	0.13
Cup shape measure	-0.50	0.11	-0.47	0.12
RNFL average (µm)	-0.34	0.30	-0.22	0.51

OCT = Optical coherence tomography, HRT = Heidelberg retina tomograph, GDx = Laser polarimetry, RNFL = Retinal nerve fiber layer, CFT = Central foveal thickness, TSNIT = Temporal-superior-nasal-inferior-temporal, NFI = Nerve fiber indicator, MD =median deviation, PSD = pattern standard deviation. $p < 0.05$ indicates statistically significance difference.

ters of the optic disc head and RNFL obtained by using a HRT III, OCT and GDx with global indices of conventional AP to reveal the diagnostic precision of these devices for detecting and following subjects with moderate and severe POAG.

Wollstein *et al*. [13] suggested that OCT has a closer relationship in glaucomatous progression than VF. In another study Kanamori *et al*. [14] showed that OCT has the capability to reveal early glaucomatous damage by calculating the RNFL thickness especially in the inferior quadrant. In addition, the RNFL thickness measurements were favorably correlated with the MD. In this study the measurement of inferior RNFL was significantly correlated with MD and PSD in moderate POAG patients. Regarding the severe POAG patients the measurements of superior, inferior, and average RNFL showed statistically significant correlations with MD and PSD. We observed that RNFL thickness obtained by OCT was decreased in the progression of POAG which was well correlated with MD indices. However, there was no significant correlation between OCT measurements and PSD in both moderate and severe POAG patients.

Previous studies demonstrated that macular retinal thickness and volume has been capable of revealing glaucomatous damage, nevertheless peripapillary RNFL thickness measurements showed higher sensitivity and specificity to determine VF abnormalities

[15, 16]. In this study macular retinal thickness and volume were significantly different between moderate and severe POAG patients and these measurements were not correlated with MD indices of AP.

In a previous study, Brigatti *et al*. [17] found a statistically significant correlation between optic disc parameters measured with HRT and functional measurements that were obtained with AP. Wollstein G *et al*. [18] also compared the confocal laser scanning ophthalmoscope parameters with the MD indices of AP in early glaucomatous patients. They found that MD indices were significantly correlated with the measurements of neuroretinal rim area, optic/disc area, cup/disc area ratio and optic disc area. In our study cup area, cup/disc area, cup/disc area (linear) and maximum cup depth were significantly correlated with MD in moderate POAG. In addition significant correlations were found between cup area, cup/disc area, cup/disc area (linear), average and maximum cup depth and cup shape measure in patients with severe POAG.

Previous studies demonstrated that GDx VCC system can be as sensitive as Stratus-OCT in demonstrating the RNFL thickness decrease in glaucoma. In these studies the NFI was found to be the best discriminating parameter which increases as the glaucoma progresses [19, 20]. In our study the NFI value was significantly higher in severe POAG than moderate POAG. In addition it was significantly correlated to MD in severe POAG.

Medeiros FA *et al*. [3] also evaluated the diagnostic capability of GDx VCC, HRT II, and Stratus OCT and showed similar results for all devices. Zangwill *et al*. [21] compared the ability of 3 instruments to differentiate healthy eyes from eyes which had early to moderate glaucomatous visual field defects. They found that measurements obtained with OCT and HRT achieved higher sensitivities compared to GDx. In our study OCT achieved the most correlated measurements with AP indices among the three devices in both moderate and severe POAG patients.

DeLeón Ortega *et al*. [22] found that the measurements of GDx, HRT II and Stratus OCT had high reproducibility in early glaucoma however the repeatability was worse in advanced glaucoma which is probably to conclude the use of NFI by GDx-VCC, rim area, cup area, and cup-to-disc area ratio from both HRT II and Stratus OCT in advanced glaucoma. In our study no significant correlation was found between these imaging devices and AP in patients with MD values less than -20 dB. This may probably be associated with the loss of glial tissue in the advanced glaucoma which may result the false high measurements.

CONCLUSION

OCT measurements had the highest correlations with the indices of AP in both moderate and severe POAG patients whereas HRT III had the lowest values. The correlations of all devices decreased in patients with more advanced glaucomatous damage hence AP still seems to be useful in the follow up disease progression in these glaucoma patients.

Authors' Contribution

Study Conception: MEA, MB, EG, ÖBT, SY; Study Design: MEA, MB, EG, ÖBT, SY; Supervision: MEA, MB, EG, ÖBT, SY; Funding: MEA, MB, EG, ÖBT, SY; Materials: MEA, MB, EG; Data Collection and/or Processing: MEA, MB, EG; Statistical Analysis and/or Data Interpretation: MEA, MB, EG; Literature Review: MEA, MB, EG; Manuscript Preparation: MEA, MB, EG and Critical Review MEA, MB, EG.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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