·Clinical Research·

Relationship between short-wavelength automatic perimetry and Heidelberg retina tomograph parameters in eyes with ocular hypertension

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Abstract

• AIM: To compare and correlate optic nerve head parameters obtained by Heidelberg retina tomograph (HRT) with short-wavelength automatic perimetry (SWAP) indices in eyes with ocular hypertension (OHT).

• METHODS: One hundred and forty-six patients with OHT included in the present study. All subjects had reliable SWAP and HRT measurements performed within a 2wk period. The eyes were classified as normal/abnormal according to visual field criteria and Moorfields regression analysis (MRA). Correlations between visual field indices and HRT parameters were analyzed using Pearson correlation coefficient (*r*).

• RESULTS: Twenty-nine eyes (19.9%) had SWAP defects. Twenty-nine eyes (19.9%) were classified as abnormal according to global MRA. Six eyes (4.1%) had abnormal global MRA and SWAP defects. The *k* statistic is 0.116 (*P*=0.12) indicating a very poor agreement between the methods. No statistical significant correlation between HRT and SWAP parameters was detected.

• CONCLUSION: SWAP defects may coexist with abnormalities of optic disc detected by HRT in eyes with OHT. In most eyes, however, the two methods detect different glaucoma properties.

• KEYWORDS: glaucoma; perimetry; optic disc; ocular hypertension

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INTRODUCTION

The diagnosis of glaucoma is traditionally based on the detection of signs of damage to the optic disc that are accompanied by visual field defects. Current evidence suggests that in many eyes a variable amount of damage to the optic disc may occur before visual field defects appear[1]. According to the ocular hypertension (OHT) treatment study disc change and glaucoma conversion was detected before visual field abnormalities in 57% of the patients [1]. Furthermore results of OHT treatment study have shown that several baseline Heidelberg retina tomograph (HRT) stereometric parameters or Moorfields regression analysis (MRA) outside normal limits were predictive for the development of glaucoma[2].

However the precise nature of the relationship between visual field loss and optic disc damage is poorly understood; therefore, many studies have been carried out to evaluate the correlation between HRT morphometric parameters and visual field indices [3-7]. Previous studies found a correlation between white on white perimetry (WWP) indices and HRT stereometric parameters in patients with glaucoma [4,7]. For patients with OHT conflicting evidence exists[4,7].

Blue on yellow or short-wavelength automatic perimetry (SWAP) is designed to assess the loss of sensitivity to short wavelengths. Numerous reports have suggested that SWAP may detect glaucomatous damage earlier than WWP, based on its ability to target a specific subpopulation of retinal ganglion cells, thereby limiting redundancy [8-11]. There is evidence that SWAP abnormalities precede WWP visual field loss by as much as 4 and 5y in eyes with OHT and suspected glaucoma [11]. Furthermore, SWAP has been reported to demonstrate closer agreement with early nerve fiber layer damage than WWP [11]. Previously Teesalu *et al* [12] reported that mean deviation in SWAP was well correlated with HRT parameters in patients with OHT and glaucoma. However it is a matter of debate if their results can be generalized since their study had a small number of participants.

The purpose of the present study is to compare HRT parameters with SWAP indices in eyes with OHT.

SUBJECTS AND METHODS

Consecutive patients with OHT examined in the Glaucoma Department of Athens University between November 2008 and June 2010 comprised the study population. All subjects underwent a complete ophthalmic examination including slitlamp biomicroscopy, WWP, SWAP and HRT. Approval for the study was obtained from the Ethics Committee of Athens General Hospital.

Inclusion criteria for the study were: 1) intraocular pressure >24 mm Hg on two different occasions in one eye, and intraocular pressure >21 mm Hg in the fellow eye at the time of diagnosis; 2) healthy optic nerves defined as vertical cup-disk asymmetry less than 0.2, cup-to-disk ratio less than 0.7 and intact neuroretinal rim without peripapillary hemorrhages, notches, or pallor; 3) normal Humphrey white on white visual field; 4) no history of other ocular disease or of ocular surgery; 5) best corrected visual acuity 20/20.

Exclusion criteria for the study were: 1) refractive error greater than 5.00 diopters spherical equivalent or greater than 2.50 diopters cylinder; 2) color vision defects; 3) lens opacities in slitlamp examination (Lens Opacity Classification System III 1 1); 4) eyes with tilted optic disks or extensive peripapillary atrophy.

Perimetry WWP and SWAP were measured with the Humphrey Field Analyzer II (Carl Zeiss Meditec) by means of the 24-2 full-threshold test paradigm. To save testing time, the SITA standard in WWP was used instead of the full-threshold strategy. Acceptable reliability indices for visual fields were less than 15% false positive and false negative rates and less than 20% fixation losses. Whenever a visual field did not meet the reliability criteria, it was repeated within 1mo and was included only if it then met reliability criteria. All patients had at least four visual fields performed (two standard and two short wavelength) in each eye to reduce the likelihood of a learning effect. WWP had been performed before SWAP as an inclusion criterion. SWAP was repeated within a 4mo period. One of the following criteria was used to establish abnormal WWP results: 1) a cluster of three or more adjacent points with $P<0.05$ on the pattern probability plots as compared with perimeter-defined age-matched normal controls; 2) two adjacent points with loss at $P<0.01$ or more below normal (none of which was located along the periphery or next to the physiologic blind spot); 3) a glaucoma hemifield test considered abnormal.

One of the following criteria was used to establish abnormal SWAP results [13]: 1) a cluster of four or more adjacent points with $P<0.05$ on the pattern probability plots as compared with perimeter-defined age-matched normal controls; 2) a cluster of 3 points lower than $P<0.01$ on pattern deviation plot; 3) pattern standard deviation (PSD) with $P<0.02$.

Optic Nerve Head Topography All subjects had reliable SWAP and HRT measurements performed within a 2wk period. Optic nerve head (ONH) topography measurements were carried out with HRT II (Heidelberg Engineering, GmBH, Heidelberg, Germany) with software version IR1-V1.7/4160. Details of this technique were previously published[14-19]. Subjects whose HRT II images had a standard deviation <35 μm were included in the study.

The optic disc contour line was drawn along the inner margin of the scleral ring by an experienced investigator (Pitsas C). A reference plane was automatically set 50 mm posterior to the mean height of the disc margin contour line in a temporal segment between 350 and 356 degrees.

The HRT II then calculated disc area (mm^2) and other ONH stereometric parameters. The parameters were cup and rim areas (mm^2), cup-to-disc ratio (C/D), mean and maximum cup depths (mm), height variation contour (HVC) (mm), cup shape measure, mean retinal nerve fiber layer (RNFL) thickness (mm), and RNFL cross-sectional area (mm^2). The parameters for the global disc were used in statistical analysis. HRT results were classified as normal or abnormal (borderline/abnormal) according to MRA.

Statistical Analysis The eye with the higher intraocular pressure on inclusion was used for the analysis of the results. Statistical software SPSS 16.0 for windows was used for conducting the statistical analysis. Descriptive analysis (mean, median, standard deviation, min, max) was used to describe continuous variables. Kolmogorov-Smirnov test was used to test for normality. Pearson Chi-square test was used to test whether specific categorical variables are independent of each other. Pearson's r coefficient was calculated, in order to assess the correlation of specific continuous variables and the k-statistic was used to determine the strength of agreement between abnormal HRT and SWAP. $P<0.05$ was considered significant for all statistical tests.

RESULTS

One hundred and forty-six eyes of 146 consecutive patients, 58 males and 88 females, were included in the present study. Mean age of patients was 53 ±10.5y. Mean intraocular pressure and mean central corneal thickness upon inclusion was 25 ±5.4 mm Hg and 559 ±37 μm respectively. All patients were Caucasian. SWAP visual field defects were confirmed in 29 eyes (19.9%).

Twenty-eight eyes (19.2%) were classified as borderline and twenty-nine eyes were classified as abnormal (19.9%) according to global MRA. Among eyes with SWAP visual field defects 6 (20.7%) were classified as abnormal according to global MRA, 14 (48.3%) were classified as normal according to global MRA, and 9 (31.0%) as borderline.

The k statistic is 0.116 ($P=0.12$) and thus there is a very poor agreement between the methods. Furthermore no statistical significant correlation between HRT and SWAP parameters was detected (Table 1).

Table 1 Correlation coefficient (Pearson's r) between HRT parameters and SWAP indices

HRT parameters	SWAP MD	SWAP PSD	SWAP SF	SWAP CPSD
Disk area	0.116 (*P*=0.16)	-0.2 (*P*=0.06)	-0.01 (*P*=0.59)	-0.14 (*P*=0.15)
Cup area	0.069 (*P*=0.41)	-0.1 (*P*=0.25)	-0.02 (*P*=0.82)	-0.06 (*P*=0.57)
Rim area	0.028 (*P*=0.74)	-0.08(*P*=0.36)	0.056 (*P*=0.56)	-0.1 (*P*=0.31)
Cup volume	0.088 (*P*=0.29)	-0.12 (*P*=0.14)	-0.01 (*P*=0.96)	-0.08 (*P*=0.38)
Rim volume	0.035 (*P*=0.67)	-0.04 (*P*=0.63)	0.04 (*P*=0.68)	-0.48 (*P*=0.62)
Cup/disk area	0.039 (*P*=0.64)	-0.05 (*P*=0.053)	-0.03 (*P*=0.78)	-0.01 (*P*=0.98)
Linear C/D	0.039 (*P*=0.64)	-0.05 (*P*=0.053)	-0.03 (*P*=0.78)	-0.01 (*P*=0.98)
Mean cup depth	0.099 (*P*=0.24)	-0.11 (*P*=0.19)	-0.01 (*P*=0.91)	-0.06(*P*=0.52)
Maximum cup depth	0.085 (*P*=0.31)	-0.12 (*P*=0.15)	0.048 (*P*=0.62)	-0.10 (*P*=0.28)
Cup shape measure	0.076 (*P*=0.36)	-0.01 (*P*=0.91)	-0.14 (*P*=0.14)	0.065 (*P*=0.49)
HVC	0.027 (*P*=0.75)	0.025(*P*=0.67)	-0.04 (*P*=0.65)	0.032 (*P*=0.73)
Mean RNFL thickness	0.078 (*P*=0.35)	-0.025 (*P*=0.77)	0.038 (*P*=0.69)	-0.055 (*P*=0.56)
RNFL area	0.094 (*P*=0.26)	-0.06 (*P*=0.44)	0.06 (*P*=0.53)	-0.084 (*P*=0.37)
Reference height	-0.02 (*P*=0.83)	0.048 (*P*=0.57)	0.025 (*P*=0.79)	0.083 (*P*=0.38)
TSD	-0.01 (*P*=0.51)	-0.04 (*P*=0.59)	0.048 (*P*=0.61)	-0.11 (*P*=0.26)

SWAP: Short-wavelength automated perimetry; MD: Mean deviation; PSD: Pattern standard deviation; SF: Short fluctuation; CPSD: Corrected pattern standard deviation; C/D: Cup/disk; HVC: Height variation contour; RNFL: Retinal nerve fiber layer; TSD: Topography standard deviation.

DISCUSSION

Several data indicate that early detection and treatment of the glaucomatous damage may benefit the clinical course of the disease. Whether structural or psychophysical methods or a combination of both should be used for this purpose remains a matter of debate [20-22]. The present study applied two technique one structural and one functional with good sensitivity and specificity in detection of early glaucomatous damage in a cohort of patients with OHT and investigated on the level of agreement among these 2 techniques in classifying eyes as normal or abnormal.

The present study indicated that among patients with OHT 19.9% had abnormal HRT based to MRA. Similarly to the present study Strouthidis *et al* [23] indicated that 20.1% of patients of patients with OHT had global MRA outside normal limits. An abnormal global MRA classification was associated with a 2-fold increased risk of either HRT or visual field progression.

Approximately 20% of eyes had SWAP defects. Polo *et al* [10] detected SWAP defects in 36% of their patient population with OHT. After at least three years of follow up WWP defects developed in 19% of patients with SWAP defects, as opposed to only 4% of eyes with normal SWAP results at baseline.

However, the present study indicated that only six eyes with OHT (4.1%) and abnormal HRT had also SWAP visual field defects. Several previous studies investigated the possibility of early structural damage and SWAP defects in patients with OHT and normal WWP. Ugurlu *et al* [24] reported structural damage and SWAP defects in 16.7% of eyes with suspected or early glaucoma. Georgopoulos *et al* [25] reported that 14.6% of eyes with OHT had abnormal SWAP and abnormal scanning laser polarimetry (SLP).

The present study indicated poor agreement between the two examined methods SWAP and HRT. Contrary to the present study Teesalu *et al* [12] reported that mean deviation in SWAP was well correlated with HRT parameters in patients with OHT. However their study included only 10 patients with OHT and 27 patients with various stages of glaucoma and their patient population with OHT was significantly older (mean age 56.3y) than patients included in the present study. Furthermore in the discussion the authors acknowledged that the correlations were not very strong and that if advanced glaucoma patients were eliminated from the data set, correlations were considerably reduced.

Similarly to the present study Bozkurt *et al* [6] reported fair agreement between HRT and frequency doubling perimetry although their patient population included patients with primary open angle glaucoma with more advanced disease than our patient population.

There are many explanations for this finding: 1) as the two instruments measure different glaucoma properties, the lack of close association between the two methods one structural and one functional may merely reflect the fact that the first detectable change of the disease may be either structural or functional depending stage of the disease or patient factors. 2) A second possible explanation is that analysis of ONH with HRT is not as sensitive method of detecting early structural damage as is analysis of nerve fiber layer with optical coherence tomography (OCT) or SLP. Georgopoulos *et al* [25] reported statistically significant correlation between SLP "number" parameter and SWAP PSD and corrected PSD. Bowd *et al* [26] displayed that among Stratus OCT, HRT II, and GDx variable corneal compensation, OCT RNFL thickness had the strongest association with visual field sensitivity. Furthermore Leung *et al* [27] indicated that

Spectralis OCT RNFL measurement attained higher sensitivity in glaucoma detection than HRT optic disk measurement. It is well known that optic disk size influences the diagnostic performance of HRT with larger discs associated with higher sensitivities and lower specificities[28,29]. 3) Another possible explanation for the discordance between RNFL and HRT neuroretinal rim measurements is that neuroretinal rim also comprises nonneural connective and supporting tissues. If loss of nonneural tissues is not synchronized with neuronal damage, it is likely that the agreement between neuroretinal rim loss and RNFL may be poor[30]. Finally there are at least two well documented studies indicating that SWAP may not be sensitive enough to detect functional damage before WWP [31,32]. Other methods of perimetry may be more sensitive than SWAP to detect early functional damage[33].

Despite the poor agreement between the two methods, abnormalities in HRT and SWAP may confer to a minority eyes an increased risk for glaucoma. Although there are not yet enough data to support the notion that abnormalities in both HRT and SWAP increase the risk for the development of glaucoma there are studies indicating that a combination of structural and functional data increases sensitivity and specificity of glaucoma diagnosis[20,34].

In conclusion the present study investigated the correlation of HRT and SWAP parameters in patients with OHT. In a small number of eyes SWAP visual field defects coexisted with abnormalities of optic disc detected by HRT. In most eyes, however, the two methods detected different glaucoma properties.

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