ARCH SOC ESP OFTALMOL 2006; 81: 135-140 **ORIGINAL ARTICLE**

SECTOR-BASED ANALYSIS OF THE DISTRIBUTION OF THE NEURORETINAL RIM BY CONFOCAL SCANNING LASER IN THE DIAGNOSIS OF GLAUCOMA

ANÁLISIS DE LA DISTRIBUCIÓN DE ANILLO NEURORRETINIANO POR SECTORES MEDIANTE LÁSER CONFOCAL DE BARRIDO EN EL DIAGNÓSTICO DEL GLAUCOMA

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ABSTRACT

Purpose: To evaluate the diagnostic ability of the Moorfields regression analysis (MRA; neuroretinal rim sector-based analysis) by means of confocal scanning laser.
Methods: 200 eyes were included in this study: 101 normal subjects and 99 glaucoma patients (standard automated perimetry with glaucomatous defects - MD or CPSD with p<0.02 or a cluster of three or more points with p<0.05 or a cluster of two or more points with p<0.01 or abnormal Glaucoma Hemifield Test). All subjects underwent a full ophthalmic evaluation, visual field evaluation by means of a Humphrey Field Analyzer, 24-2 full threshold strategy, and optic disc topography by Heidelberg retina tomograph (HRT-II). The outcome parameters were sensitivity and specificity of the MRA for each sector.
Results: The highest sensitivity in detecting structural defects based on MRA (p<0.05) was observed in the nasal-superior sector (48%) and nasal-inferior sector (45%); however the highest specificity

RESUMEN

Objetivos: Valorar la capacidad diagnóstica del análisis de la distribución de anillo neurorretiniano por sectores (regresión de Moorfields, MRA), medido mediante láser confocal de barrido.
Material y métodos: Se estudiaron 200 ojos, de los cuales 101 eran normales y 99 glaucomas clasificados por una perimetría automatizada convencional con defectos glaucomatosos (DM o DSPC con p<2% o grupo de 3 puntos con p<5% o 2 con p<1% o Glaucoma Hemifield Test alterado). A todos ellos se les realizó exploración oftalmológica completa, PA Humphrey 24-2 umbral completo y una topografía papilar con HRT-II. Se calculó la especificidad y la sensibilidad de los resultados de la clasificación MRA para cada uno de los sectores.
Resultados: Se observó mayor sensibilidad para detectar defectos estructurales basados en MRA (p<0,05) en los sectores nasal superior (48%) y nasal inferior (45%), mientras que la mayor especificidad se encontró en los sectores temporal superior (98%) e inferior (98%). La mayor sensibilidad

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was found in the temporal-superior (98%) and inferior (98%) sectors. The highest sensitivity for MRA ($p<0.01$) was found in the temporal-inferior sector (31%) and nasal-superior sector (30%) while the temporal-superior and inferior-sectors showed the highest specificity (100%).
The diagnosis of glaucoma based on the presence of any sector alteration showed sensitivity figures of 67% with $p<0.05$ and 46% with $p<0.01$ and specificity values of 84% with $p<0.05$ and 96% with $p<0.01$.
Conclusions: The analysis of the distribution of the neuroretinal rim by means of HRT-II contributes effectively to the diagnosis of glaucoma based on perimetry in a sample derived from a Spanish population *(Arch Soc Esp Oftalmol 2006; 81: 135-140).*

Key words: Glaucoma, diagnosis, HRT, optic nerve head.

para una MRA p<0´01 se obtuvo en el sector temporal inferior (31%) y nasal superior (30%), y la mayor especificidad en los sectores temporales superior e inferior y nasal inferior (100%). El diagnóstico de glaucoma basado en la afectación de uno o más sectores reveló una sensibilidad de 67% para una p<0,05 y 46% para una p<0,01 y una especificidad de 84% para una p<0,05 y 96% para una p<0,01.
Conclusiones: El estudio de la distribución del anillo neurorretiniano con el HRT-II contribuye eficazmente al diagnóstico de glaucoma perimétrico en una muestra de población española.

Palabras clave: Glaucoma, diagnóstico, HRT, nervio óptico.

INTRODUCTION

At present, chronic open-angle glaucoma is one of the main causes of blindness in the world. The damage it causes in the optic nerve is characterized by the progressive loss of retinal ganglionar cells which gives rise to defects in the visual field. This ganglion cells loss gives rise to structural changes in the head of the optic nerve and to the thinning of the retina nerve fiber layer (1,2). Due to the irreversible nature of the damage, early diagnosis of the process is of vital importance. At present, it seems to be accepted that the detection of structural changes of the optic nerve precede the appearance of functional deterioration in the visual field (3-6). In this context, the assessment of the papilla by means of a papillar CAT scan made with the Heidelberg Retina Tomograph (Heidelberg Engineering GMBH, Dossenheim, Germany) (HRT-II) has demonstrated in many studies to be useful in the diagnostic of said structural changes (1-10). HRT-II is a precise, fast and reproducible diagnostic method which provides a large amount of quantitative parameters about the morphology of the optic disc (11-13). In order to facilitate the interpretation of these data, diagnostic algorithms have been developed such as that proposed by the Moorfields hospital which, based on a normality value, establishes a linear regression between the neuroretinal ring and the optic disc area as a function of age (1).

The objective of this study is to assess the diagnostic capacity of the neuroretinal ring distribution, globally and by sectors, measured with confocal scan laser in a sample of the Spanish population.

SUBJECTS, MATERIAL AND METHODS

Subjects

This study included 200 eyes selected consecutively in the glaucoma unit of the Ophthalmology Service of our hospital. The eyes were classified into groups: Normal and glaucomatous. The selection of the included eye was random, excepting the cases in which only one eye fulfilled the inclusion criteria.

We considered as normal eyes those with an IOP below 21 mmHg in at least two explorations, 1 normal ophthalmological exploration and 1 normal conventional automated perimetry. As regards the eyes diagnosed with open angle glaucoma, their basal intraocular pressure was over 21 mmHg in at least two explorations and one conventional automated perimetry with glaucomatous defects.

All patients were selected on the basis of the following inclusion criteria: age between 30 and 80, visual acuity equal or over 8/10 in the Snellen scale, refraction defects below 5 lens dioptries and/or astigmatism below 3 dioptries of lens equivalent, and transparent optical media.

The patients excluded from the study were all those having serious hematological or cardiovascular diseases, history of traumatism or surgery, retinopathy of any origin, angular abnormalities or impossibility of carrying out any of the tests included in the exploratory protocol. All the subjects included in the study were requested to sign an informed consent for carrying out the explorations.

Conventional automated perimetry

The automated perimetry (PA) was made with the Humphrey Field Analyzer (mod. 754, Humphrey Zeiss Instruments) following a full threshold strategy and utilising programme 24-2 which explores the 24 most central degrees of the visual field. The results were analysed and interpreted utilising the statistical package (STATPAC 2) of the perimeter. For the study, the third visual field was selected with perimetries carried out in a three-month period without medical occurrences which could alter the results.

The criteria followed to define a perimetry with glaucomatous damage were: mean deviation (DM) or corrected pattern standard deviation (DSPC) with p<2% and/or group of 3 or more adjacent points with a probability level below 5% and/or group of two or more of adjustment points with a probability level below 1% (not located in the peripheral crown of the visual field or in the vertices of the blind spot) and/or altered Glaucoma Hemifield Test alterado.

Confocal laser scan HRT II

A Heidelberg Retina Tomograph (HRT-II) confocal laser scan was utilised to carry out a papillar topographic study on all patients. In all cases, the scan was made under mydriasis with tropicamide.

The confocal laser scan is a precise, reproducible and fast diagnostic method. HRT II (Heidelberg Engineering, Gmbh, Heidelberg, Germany) includes a papillar analysis programme (Heidelberg Eye Explorer version 1.3.0.0) which determines, calculates and analyses multiple structural morphometric parameters of the optic nerve. In this way, starting from the papillar contour and the plane of reference, the programme provides morphometric quantitative results of multiple papillar parameters (disc area, ring area, excavation volume, thickness of the retina nerve fibre layer, etc.). In what concerns these papillar parameters, the HRT-II allows for global or sectoral evaluation and analysis. In order to carry out the partial analysis the topographic image of the optic nerve is divided in the following papillar regions: temporal-superior, temporal, temporal-inferior, nasal-superior, nasal and nasal-inferior. In this way, all the parameters are established, calculated and analysed for each sector.

HRT-II also includes an analysis of the neuroretinal ring (Moorfields regression analysis). It compares the values of the neuroretinal ring area (globally and per sector) of a subject assessed with a normality value is included in the study, corrected for age and size of the papilla. In this way, the analysed papilla are classified as normal, pathological or suspect depending on the neuroretinal ring values of the evaluated subjects being within the confidence interval of 95%, outside the 99.9% interval or between both confidence intervals of the distribution of normality.

Statistical Analysis

A cross-section observation study was designed, calculating the sensitivity and specificity of the neuroretinal ring area and analysis according to the results of the Moorfields base (globally and per sector) for diagnosing glaucoma. Finally, an analysis was carried out considering as normal the presence of all normal sectors and as pathological an alteration in any of said sectors. The statistical programme utilised for this analysis was SPSS 11.0 for Windows (SPSS inc., Chicago, USA).

RESULTS

In this study, 200 eyes were analysed of which 101 were normal and 99 glaucomatous, as a function of a conventional automated perimetry. The descriptive characteristics of both sample populations are found in table I.

Considering as normal the neuroretinal rings included in the confidence interval of 95% of the distribution of normality (corrected for age and papillar size), it was observed that the more specific sectors for the diagnostic of glaucoma were the temporal-superior and inferior sectors (specificity of 98.02%) and the more sensitive were the nasal-superior and inferior sectors (sensitivity of 48.48% and 45.45% respectively). The global analysis showed a specificity of 96.04% and a sensitivity of 47.47% and any altered sectors were considered to be pathological, giving a specificity of 84.16% and a sensitivity of 67.67%. Table II shows all the sensitivity and specificity data obtained for each sector and globally, considering a confidence interval of 95% of distribution of normality.

For a confidence interval of 99.9%, the sectors which on their own were proved to be more specific were the temporal-superior, temporal-inferior and nasal-inferior (specificity of 100%) and the most sensitive sectors were nasal-superior and -inferior (sensitivity of 30.30% and 29.29% respectively). The global analysis of the neuroretinal ring provided a specificity of 99.01% and a sensitivity of 29.29%. Considering as pathological the presence of any altered sector, specificity was of 96.04% and sensitivity 46.46%. Table III shows sensitivity and specificity data obtained by sector and global analysis of the neuroretinal ring considering a confidence interval of 99.9% of normality distribution.

Table I. Descriptive characteristics of sample populations

	CONTROL (n=101)	GLAUCOMA (n=99)
Age	55,5 of 12.7	57.9 of 9.7
VA	0.8 of 0.1	0.8 of 0.1
IOP basal	14.6 of 2.8	24.2 of 4.5 (*)
E/P	0.8/5 of 0.8/5	3.4/5 of 1.1/5 (*)
MD (CC)	-0.56 of 1.5	-6.8 of 6.8 (*)
CPSD (CC)	1.03 of 1.1	4.95 of 3.7 (*)

* Statistically meaningful differences between the two groups. VA: visual aquity; IOP: intraocular pressure; E/P: proportion excavation/papilla; DM: mean deviation; CPSD: corrected pattern standard deviation; DE: standard deviation.

DISCUSSION

The structural analysis of the head of the optic nerve is essential in the diagnosis of simple chronic glaucoma. In this regard, in recent years several instruments have been developed for a morphological study thereof (14,15).

O´Connor et al (16) compared different methods for diagnosing glaucoma damage in the optic disk and concluded that the greater sensitivity (72%) and specificity (87%) were obtained by exploration with stereophotographs of the head of the optic nerve. For this reason, it has been considered as the best method for detecting secondary changes of glaucoma in the papilla.

HRT is a confocal scan laser that provides a morphological analysis of the head of the optic nerve. Numerous studies have proved that this is a highly reproducible diagnostic method (11-13).

The analysis of the neuroretinal ring by means of the Moorfields regression, which is included in HRT-II, had proved in previous studies a high diagnostic capacity in glaucoma.

Wollstein et al (3,7) described this linear regression between the area of the optic disk and the logarhythm of the neuroretinal ring area, showing that the most specific areas were temporal inferior (specificity 100%, sensitivity 62.7%) and nasal inferior (specificity of 98.8% and sensitivity of 54.9%) for a confidence interval of 99%. The sectors which evidenced greater sensitivity were temporal-inferior (62.7%) and nasal-inferior (54.9%). Considering the presence of any altered sector as pathological, a sensitivity of 84.3% and a specifi-

Table II. Results for sensitivity, specificity, positive and negative predictive value and probability reasons for the neuroretinal ring analysis with a confidence interval of 95% of normality distribution

IC Sectors 95%	Specificity	Specificity	Positive predictive value	Negative predictive value	Positive probability reasong	Negative probability reason
Nasal superior	95.05%	48.48%	90.6%	34.7%	9.79	0.54
Nasal	93.07%	32.32%	82.1%	41.6%	4.66	0.73
Nasal inferior	96.04%	45.45%	91.8%	35.8%	11.48	0.57
Temporal inferior	98.02%	43.43%	95.6%	36.1%	21.93	0.58
Temporal	95.95%	34.34%	87.2%	40.4%	6.94	0.69
Temporal superior	98.02%	43.43%	95.6%	36.1%	21.93	0.58
Global	96.04%	47.47%	92.2%	34.9%	11.99	0.55

Table III. Results for sensitivity, specificity, positive and negative predictive value and probability reasons for the neuroretinal ring analysis with a confidence interval of 99.9% of normality distribution

IC Sectors 99.9%	Specificity	Specificity	Positive predictive value	Negative predictive value	Positive probability reasong	Negative probability reason
Nasal superior	99.01%	30.30%	96.8%	40.8%	30.61	0.70
Nasal	98.02%	22.22%	91.7%	43.8%	11.22	0.79
Nasal inferior	100%	29.29%	100%	40.9%		0.71
Temporal inferior	100%	31.31%	100%	40.2%		0.69
Temporal	99.01%	8.08%	88.9%	47.6%	8.16	0.93
Temporal superior	100%	21.21%	100%	43.6%		0.79
Global	99.01%	29.29%	96.7%	41.2%	29.59	0.71

city of 96.3% was obtained. The development of the Moorfields regression model was based on a sample of 80 normal subjects in whom the specificity and sensitivity calculations were made, and 55 patients with glaucoma (all chosen without any specific sampling system of their reference population). For this reason, the true clinical value of this type of tool lies in the validation it may provide on the basis of other reference populations such as that of our ethnic and geographical environment. In our study, the aim was to determine the true value that this analysis can have in subjects within our social environment in a population independent of that utilised for the development of the model and in a higher number of cases than those utilised by Wollstein.

In our case, the segment with greater specificity and sensitivity match those described by Wollstein (adding temporal-superior with high specificity and nasal-superior with high sensitivity), although in all cases the sensitivities were markedly lower than those referred by said author. The same occurs when comparing the results of considering any altered sector as pathological.

Likewise, in the neuroretinal ring analysis at the global level, Miglior et al (1) obtained a sensitivity of 74% and specificity of 85% when comparing normal subjects and those suspect of suffering glaucoma with glaucomatous patients, and a sensitivity of 41% and specificity of 94% when comparing normal subjects with suspect and glaucomatous subjects. In the comparison of the population under study, we observed important differences in the perimetral indices, showing more advanced cases of glaucoma in Miglior's population, which could be related to the sensitivity values they obtained, which are higher than ours.

Finally, the research of Ford et al (17) shows a sensitivity of 58% and specificity of 96% when comparing normal subjects and those suspect of suffering glaucoma with glaucomatous subjects, and a sensitivity of 78% and specificity of 81% when comparing normal subjects with suspect and glaucomatous subjects.

All the above data evidenced the variability of this type of analysis according to the differences existing in the population under study, both at the demographic as well as the hospital level. In order to avoid any bias in our results, we could have assessed the size of the papilla in order to minimise its influence on the sensitivity and specificity figures.

The Multivariant Discriminating Analysis (MDA), also provided by HRT-II, has demonstrated in previous studies a high diagnostic capacity with a sensitivity of 83% and specificity of 75% (1).

A number of discriminating linear functions have been created in an effort to increase the diagnostic capabilities, such as the function of Mickelberg et al (18), Bathija et al (19) and Larrosa et al with sensitivities of 55%, 67% and 65%, respectively for a specificity of 90%.

In the light of these results, it can be concluded that HRT is a tool that carries out a morphological analysis of the retina and the head of the optic nerve which has demonstrated high diagnostic capacity for a glaucoma. However, its use must not be considered in isolation but in the context of a clinical assessment and different morphological and functional diagnostic means available at present.

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