CLINICAL STUDY

A comparative study of computerised visual field testing and optic disc morphometric parameters in the follow-up of primary open angle glaucoma

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Abstract

Purpose To evaluate the correlation between computerised visual field testing and optic disc morphometric parameters (rim area, rim/disc area ratio, cup/disc area ratio and optic disc surface smoothness (ODSS)) in the follow-up of a group of patients affected by primary open angle glaucoma (POAG).
Methods Reliable automated perimetry (Humphrey 640 VFA, central 30–2 threshold program) was performed at T_0 (the enrolment time), T_1 (after 6 ± 1 months; range 5–7 months), T_2 (12 ± 1 months), T_3 (18 ± 1 months), and T_4 (the end of the follow-up period: 24 ± 2 months) in one eye randomly chosen from each of 30 POAG patients. Computerised optic disc analysis (IMAGEnet X Rev–3–51b, Topcon Europe, The Netherlands) was performed at T_0 and T_4. To evaluate the correlation between morphometric parameters and computerised visual field testing, the stability or worsening of visual field test was evaluated by means of 'Mean Deviation linear regression analysis' (STATPAC 2 software); that of morphometric parameters was studied using their coefficients of variation. A rank of '0' was assigned to stability and a rank of '1' to worsening. The Spearman rank correlation coefficient was used to evaluate statistically the correlations between visual field analysis and morphometric parameters. Furthermore kappa statistic was used to evaluate the agreement of morphometric parameter changes with visual field progression analysis.
Results According to the MD slope regression analysis, in 18 patients the visual fields were stable while in 12 they were worsening during the follow-up period. In 86.65% of patients ($n = 26$) the morphometric parameter ODSS and visual field analysis were concordant ($p < 0.0001$). In 80% of patients ($n = 24$) the cup/disc area ratio and visual field analysis were concordant ($p < 0.001$). The other morphometric parameters (rim area, rim/disc area ratio) were less correlated with visual field analysis than ODSS ($p < 0.05$). The agreement of visual field analysis with all the morphometric parameters was good (kappa = 0.690, 95% confidence interval (CI) of kappa = 0.589–0.790). The agreement of visual field analysis with ODSS and cup/disc area (kappa = 0.688; 95% CI = 0.511–0.864) was better than the agreement of visual field analysis with rim area and rim/disc area ratio (kappa = 0.438; 95% CI = 0.260–0.655).
Conclusion Analysis of the progression of visual field damage and optic nerve head morphometric parameters should both be taken into account in glaucoma follow-up. Among the morphometric parameters evaluated by means of Topcon IMAGEnet, ODSS and (to a lesser extent) the cup/disc ratio should have the greatest weight.

Key words Automated visual field, Disc area, Glaucoma, Mean deviation, Mean deviation linear regression analysis, Optic disc

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Although the importance of optic disc morphometric analysis in glaucoma follow-up is widely accepted, its ability in forecasting or indicating typical functional impairment is unclear. In particular, the correlation between the morphometric optic disc values and differential light sensitivity as detected by visual field testing is poorly defined.

The aim of this study was to evaluate the correlation between computerised visual field testing and optic disc morphometric parameters (rim area, rim/disc area ratio, cup/disc area ratio and optic disc surface smoothness) in the follow-up of a group of patients affected by primary open angle glaucoma (POAG).[1–7]

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Table 1. *Characteristics of the patients at enrolment (T_0)*

Age (years)	69.5 ± 7.7
Male/female	11/19
Rim area (mm^2)	1.1 ± 0.4
Rim/disc area ratio (mm^2)	0.4 ± 0.1
Cup/disc area ratio (mm^2)	0.75 ± 0.1
Mean deviation (dB)	−8.9 ± 9.5
Corrected pattern standard deviation (dB)	7.9 ± 6.5

Values are the mean ± SD.

Methods

Thirty consecutive patients were recruited into the study for a period of 24 ± 2 months (range 22–26 months). The patients were selected from those monitored for glaucoma at the Glaucoma Service of the Department of Ophthalmology of the University of Genoa (Table 1).

Inclusion criteria were: (1) absence of refractive defects > ± 3 dioptres; (2) possibility of obtaining good pupillary mydriasis > 7 mm; (3) absence of systemic and/or ocular diseases capable of modifying the papillary surface (diabetes, hypertension, vasculitis, other primary and/or secondary vascular diseases, optic neuropathy except glaucoma, etc.); (4) absence of optic media opacities blocking good image acquisition; (5) presence at two or more measurements of an intraocular pressure higher than 21 mmHg without therapy; (6) open angle at gonioscopy; (7) ability to obtain a reliable Humphrey visual field using program 30–2 (less than 30% false positive and false negative responses and fixation loss less than 10%); (8) presence of typical glaucomatous visual field defects on computerised perimetric testing determined by at least: (a) two continuous points with 10 dB loss or greater in the superior or inferior Bjerrum areas when compared with perimeter defined age-matched controls, (b) three contiguous points with 5 dB loss or greater in the superior or inferior Bjerrum areas, or (c) a 10 dB difference across the nasal horizontal mid-line in two or more adjacent locations;[8,9] (9) previous experience in performing an automated visual field test. During these 2 years of follow-up all patients had treatment to reduce the intraocular pressure as much as possible.

To study optic disc morphology and to obtain morphometric values simultaneous stereoscopic videographic pictures were used. Three stereoscopic images of the optic nerve were taken from one randomly chosen eye from each patient by using the IMAGEnet X Rev–3.51b Topcon system (Topcon Europe, The Netherlands) at T_0 (the enrolment time) and T_4 (the end of the study, i.e. 24 ± 2 months later). This Topcon system included two charge-coupled device video cameras that also had a green separation system to help delineate the topography of the optic disc. The analogue signals from both cameras travelled to the red and green analogue-to-digital converters. The final digital images (512 × 512 × 24 bit image memory) were then displayed and could be saved to disk. Correction for magnification errors was provided by means of correction factors based on the Littmann formula that were implemented in the software.[10]

The 'Optic Disc Analysis' program was applied to each optic disc image: after identifying four points located on the external edge of the optic disc rim, this program allowed calculation of standard morphometric parameters such as rim area, disc area, rim/disc area ratio (RA/DA), cup/disc ratio (C/D) and also the position of a large number of points with respect to an arbitrarily chosen plane (the number of points depending on the size of the disc area) located across the entire surface of the optic nerve head and defined as optic disc surface smoothness (ODSS).[1] ODSS reflects the three-dimensional shape of the optic nerve head and was studied taking into account the differences of the relative position of the points which identified the optic disc surface. It was calculated by measuring the standard deviation (SD) from the mean height of the points (n_p) that identify the optic disc surface multiplied by −1: [ODSS = −1 × SD (n_p)]. The reproducibility of the technique has been evaluated in a previous study.[1]

The coefficients of variation of the morphometric parameters were calculated from the three images of the same optic nerve head and then the mean (of all the eyes considered in the study) was determined (coefficient of variation = standard deviation/mean × 100). The coefficient of variation of ODSS has already been calculated in a previous paper, when it was found to be 10.4%;[1] however, it was calculated again in this study to allow comparison with the other coefficients of variation calculated on the same sample.

Automated perimetry (Humphrey 640 VFA, central 30–2 threshold program) was performed on the same day as the optic disc measurement or within 7 days of the image recording (T_0) and at T_4 (24 ± 2 months, range 22–26 months). Furthermore a visual field test was also performed at T_1 (after 6 ± 1 months), T_2 (12 ± 1 months) and T_3 (18 ± 1 months) to allow 'Mean Deviation (MD) linear regression analysis' (STATPAC 2 software). Statistical analysis was performed on the data obtained during these examinations (T_0, T_1, T_2, T_3, T_4) by selecting the option 'Glaucoma Change Probability' included in the STATPAC 2 software. This function allows the results from two or more consecutive perimetric examinations to be compared and the statistical significance of variations to be evaluated. A MD linear regression analysis was also executed by this program and the message 'MD slope significant' or 'MD slope not significant' appeared on the printout at the end of each run. In this study, progressive worsening of the visual field was considered to be present when the message 'MD slope significant' appeared.

To evaluate the progression of the anatomical damage the coefficient of variation of each morphometric parameter was considered, that is a change was considered as a 'true' (significant) only if larger than two coefficients of variation.

A rank of '0' was assigned to glaucoma 'stability' and a rank of '1' to 'worsening'. The Spearman rank correlation coefficient was used to statistically evaluate the correlation between computerised visual field testing and changes in a morphometric parameter. In addition

Table 2. *MD slope regression analysis (95% confidence interval (CI) as shown by Humphrey 'MD slope regression analysis' software) and percentage changes in ODSS, C/D, RA and RA/DA*

Patient no.	MD slope 95% CI	ODSS (%)	C/D (%)	RA (%)	RA/DA (%)
1	0.32 ± 2.66	12	9	−11	−11
2	−1.2 ± 1.79	8	12	−10	−12
3	−0.57 ± 1.83	6	11	−8	−10
4	−1.13 ± 0.94	9	−6	−8	7
5	0.15 ± 1.3	7	10	**(−29)**	**(−24)**
6	−1.06 ± 1.47	18	9	−9	−8
7	−0.85 ± 1.85	3	8	**(−30)**	**(−25)**
8	0.23 ± 1.96	9	10	−10	−17
9	−0.32 ± 2.02	10	11	−12	−10
10	−1.11 ± 1.62	2	12	−8	−11
11	−0.71 ± 1.83	−1	−5	−7	−12
12	0.21 ± 2.18	4	**(30)**	4	−9
13	−1.01 ± 1.36	6	23	−10	−15
14	−0.47 ± 0.61	−3	10	−11	−9
15	0.06 ± 0.17	9	**(28)**	**(−29)**	**(−24)**
16	−0.15 ± 0.25	10	20	**(−28)**	**(−26)**
17	−0.25 ± 0.63	**(22)**	**(27)**	**(−25)**	**(−24)**
18	−0.76 ± 1.35	**(24)**	**(27)**	**(−26)**	**(−25)**
19	−1.71 ± 1.07	**(12)**	**(18)**	−33	−24
20	−0.24 ± 0.13	**(15)**	**(20)**	−32	−25
21	−1.32 ± 0.46	24	28	−29	−27
22	−4.60 ± 1.41	30	30	**(−22)**	**(−18)**
23	−2.15 ± 1.04	25	33	−28	−30
24	−3.54 ± 1.76	22	34	−30	−31
25	−0.48 ± 0.18	23	28	**(−18)**	**(−13)**
26	−0.76 ± 0.25	26	27	**(−23)**	−26
27	−1.13 ± 0.67	23	30	−25	**(−16)**
28	−2.36 ± 1.08	22	29	−26	−25
29	−0.35 ± 0.11	25	27	−27	−30
30	−0.66 ± 0.18	24	35	−31	−26

Note that the first 18 patients are those with a stable visual field, while the last 12 are those whose visual field is worsening. The bold values in parentheses for ODSS, C/D, RA and RA/DA are the values not concordant with MD slope regression analysis.

the kappa statistic was used to study the agreement in glaucoma follow-up evaluation between the changes in morphometric parameters (ODSS, C/D, RA, RA/DA) and analysis of the progression of visual field damage (MD slope regression analysis).

Results

According to the MD slope regression analysis, 18 patients had stable visual fields while 12 had visual fields that worsened during the follow-up period.

Regarding the morphometric parameters, an increase in ODSS of more than 21% was considered a real worsening (that is, 2× coefficient of variation (CV) = 10.5% × 2). A change in RA of greater than 24% was considered a real change (CV = 12%). Equally a decrease in RA/DA of more than 23% was considered a real change (CV = 11.5%). As 13% was the CV of C/D, an increase of more than 26% was considered a real change in this parameter.

The rough data for each patient regarding the MD slope regression analysis and its 95% confidence interval, and the percentage change during the follow-up period in ODSS, C/D, RA, and RA/DA are shown in Table 2. In 86.65% of patients ($n = 26$) ODSS and visual field analysis were concordant ($p < 0.0001$). In 80% of patients ($n = 24$) the C/D and visual field analysis were concordant ($p < 0.001$). The other morphometric parameters (rim area, rim/disc area ratio) were less well correlated with visual field analysis than ODSS ($p < 0.05$) (Tables 3, 4). The agreement between visual field progression and all the morphometric parameters was good (kappa = 0.690; 95% confidence interval (CI) of kappa = 0.589–0.790). The agreement between visual field progression and ODSS and C/D (kappa = 0.688; 95% CI = 0.511–0.864) was

Table 3. *Spearman rank correlation coefficients (r), 95% confidence intervals (CI) and statistical significance (p) between the morphometric parameters rim area (RA), rim/disc area ratio (RA/DA), cup/disc area ratio (C/D) and optic disc surface smoothness (ODSS) and computerised visual field test analysis (VF)*

	RA	RA/DA	C/D	ODSS
VF	$r = 0.41$	$r = 0.41$	$r = 0.60$	$r = 0.72$
95% CI	0.05–0.68	0.05–0.68	0.29–0.79	0.48–0.86
p	<0.05	<0.05	<0.001	<0.0001

Table 4. *Percentage agreement between MD slope regression analysis and changes in ODSS, C/D, RA, RA/DA*

% agreement	ODSS	C/D	RA	RA/DA
Visual field	86.65	80	70	70
ODSS	—	93.33	66.67	66.67
C/D	93.33	—	70	70
RA	66.67	70	—	96.67
RA/DA	66.67	70	96.67	—

Note that a change in any morphometric parameter was considered as significant only if the change was larger than two coefficients of variation.

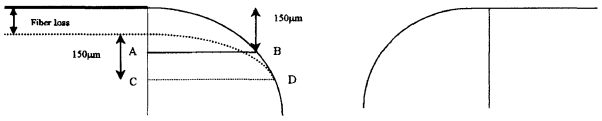

Fig. 1. *The rim area of a healthy optic disc is measured by considering the interior rim edge as defined by points located 150 μm under the nerve fibre surface (represented by the continuous segment A–B). Dotted lines represent the new shape of the optic nerve head after loss of nerve fibres. The dotted segment C–D is the rim area (again considering the interior rim edge as defined by points located 150 μm under the nerve fibre surface) after a loss of fibres. Note that C–D is larger than A–B. Use of such a rim area measurement might therefore mask a reduction occurring as a result of fibre loss. This could represent a considerable bias in judging the progress of the disease overall in early glaucoma.*

better than that between visual field analysis and rim area and rim/disc area ratio (kappa = 0.438; 95% CI = 0.260–0.655).

Discussion

The early detection of glaucomatous damage could be improved by the use of several computerised instruments able to better evaluate peripapillary area and optic disc morphometry.[1,11–15] Many authors have demonstrated significant correlations between optic disc morphometry and visual field damage.[16–20] These data suggest that visual field damage can be detected by optic nerve head analysis also. Since Quigley *et al.*[21] and Pederson *et al.*[22] first showed that optic nerve head damage could precede visual field defects, many authors have tried to detect early damage using only optic nerve head evaluation by computerised systems. Many of these computerised instruments for optic disc morphometry offered reasonably reliable measurements of the three-dimensional shape of the optic nerve head that could be used clinically in place of the traditional bi-dimensional parameters such as rim area, disc area, rim/disc area ratio and cup/disc ratio.[1,13–15] Nevertheless the clinical relevance of computerised and non-computerised optic disc analysis in glaucoma follow-up is still a matter of debate.[2–7,15]

On the other hand the sensitivity of automated perimetry in detecting the progression of damage in POAG follow-up is not clear;[23–28] in particular in spite of the good sensitivity and acceptable specificity of commercially available analytic algorithms (STATPAC 1 and 2) found by Katz *et al.*[25] for the detection of visual field progression, Birch *et al.*[28] showed a low level of agreement in a study of glaucomatous visual field damage progression by means of three different algorithms (Glaucoma Change Probability, Linear Regression Analysis, Progressor Programme).

The functional and morphometric findings in our group of patients showed a correlation (Table 3) between visual field testing and all morphometric optic disc parameters (ODSS, C/D, RA, RA/DA). This was confirmed by the kappa statistic (kappa = 0.690, 95% CI kappa = 0.589–0.790). The three-dimensional morphometric parameter ODSS was much better correlated with visual field progression in glaucoma

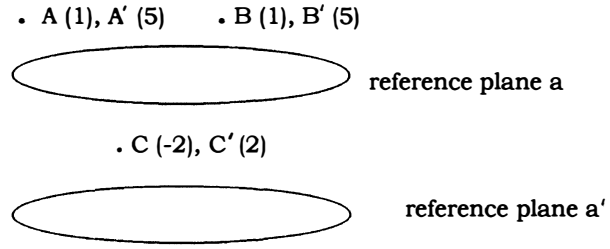

Fig. 2. *Standard deviation measurements of optic disc surface are less influenced than the arithmetic mean by reference plane location. If we consider the position of three different points (A, B, C) related to the reference plane* a *(points A = 1, B = 1, C = −2) and related to the parallel reference plane* a′ *(points A′ = 5, B′ = 5, C′ = 2), the arithmetic mean changes according to the plane location (related to the plane* a*: mean = (+1+1−2)/3 = 0; related to the plane* a′: mean = *(+5+5+2)/3 = 4), while the standard deviation is independent of the reference plane position (SD = 1.73 for both* a *and* a′*).*

follow-up than two of the classic bi-dimensional parameters (RA, RA/DA), while it was comparable with (but a little better than) C/D (Table 3). This was supported by the concordance of ODSS and C/D with visual field progression (kappa = 0.688; 95% CI = 0.511–0.864), which was better than the concordance of visual field analysis with rim area and rim/disc area ratio (kappa = 0.438; 95% CI = 0.260–0.655).

The explanation of this could be in the fact that in the Topcon IMAGEnet rim area measurement, and in particular the definition of the internal edge of the rim, is done automatically (as in many other computerised systems), by taking into consideration the group of points 150 μm under the plane located on the external edge of the rim. In early glaucomatous damage a loss of fibres could cause a decrease in height of the retinal nerve fibre layer so that the computerised system will redefine the internal edge of the rim. The new localisation might not be more external than the previous one (Fig. 1). Thus, using this computerised system, apparently there is not always a correspondence between loss of fibres and a decrease in the rim area, which could lead to the computer not registering any change in an area in spite of a loss of retinal nerve fibres (Fig. 1). In contrast, ODSS is the result of the evaluation of the position of a large number of points located on the surface of the optic disc and is thus supposed to be less influenced by reference plane location (Fig. 2) than the traditional bi-dimensional morphometric optic disc parameters.[1,14]

In conclusion, analysis of the progression of visual field damage and changes in optic nerve head morphometric parameters should both be taken into account in glaucoma follow-up. In particular, of the morphometric parameters evaluated by means of Topcon IMAGEnet, ODSS and (to a slightly lesser extent) C/D should have the greatest weight.

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