IMAGE ANALYSIS OF THE OPTIC NERVE HEAD IN PATIENTS WITH UNILATERAL VISUAL FIELD LOSS ASSOCIATED WITH OPEN ANGLE GLAUCOMA*

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INTRODUCTION

The advent of computerized perimetry in glaucoma has shifted attention from measurements of aqueous humor dynamics to functional measurements of glaucomatous optic nerve damage. However, the available data suggests that perimetric abnormalities may be preceded by structural alterations of the optic nerve head. Studies of the optic nerves of patients at risk for developing visual field loss from glaucoma are required to find the earliest clinical signs of glaucomatous optic nerve damage. Such studies are slowed by the low incidence of visual field loss in patients at risk. Primary open angle glaucoma is not infrequently an asymmetric disease; patients with unilateral visual field loss constitute a group with a relatively high risk for the future development of visual field abnormalities.

We used computerized image analysis to study quantitatively the optic nerves of patients with unilateral visual field loss from primary open angle glaucoma to gather additional information regarding the structural characteristics of the optic nerve in early glaucoma, and to provide a baseline for future prospective evaluation.

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METHODS

The records of patients of the Yale Eye Center Glaucoma Service who had computerized topographic analysis of the optic nerve head (Rosenstock Analyzer) and Octopus computerized perimetry (Program 32) were reviewed. Program Delta provided estimates of total visual field loss. Patients were included in the study if they met the following criteria:

1. Computerized optic nerve image analysis and Octopus perimetry were performed within one month of each other;

2. Program 32 of the Octopus perimeter revealed a definite scotoma consistent with glaucomatous visual field loss in one eye (total loss > 80 decibels) and no scotomas or significant depression of the visual field in the contralateral eye (total loss < 40 decibels);

3. There was an absence of visually significant cataract; and

4. The patient had a clinical diagnosis of primary open angle glaucoma without evidence of pseudoexfoliation, pigmentary dispersion, angle recession, or other forms of secondary glaucoma.

Quantitative optic nerve head measurements were also made on an age- and sex-matched normals to provide a control group. These subjects had no evidence of eye disease, consisted of volunteers or spouses of patients, and were not patients who had come to the Eye Center for evaluation.

Figure 1. - Gray scale representation of the visual field (Octopus Program 32) and optic disc photograph in a) the right eye and b) the left eye of a typical patient in the asymmetric primary open angle glaucoma group.
### TABLE. Values for eyes with normal and abnormal visual fields (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Normal Visual Field</th>
<th>Abnormal Visual Field</th>
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<tbody>
<tr>
<td>Visual Acuity</td>
<td>0.86 ± 0.06</td>
<td>0.87 ± 0.05</td>
</tr>
<tr>
<td>Refractive Error</td>
<td>+0.40 ± 0.49</td>
<td>+0.25 ± 0.63</td>
</tr>
<tr>
<td>(Spherical Equiv, Dipters)</td>
<td></td>
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<tr>
<td>Intraocular Pressure</td>
<td>20.1 ± 0.8</td>
<td>20.7 ± 0.8</td>
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<tr>
<td>(mm Hg)</td>
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<tr>
<td>VISUAL FIELD</td>
<td></td>
<td></td>
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<tr>
<td>Pupil Size</td>
<td>4.3 ± 0.4</td>
<td>3.7 ± 0.4</td>
</tr>
<tr>
<td>(mm²)</td>
<td></td>
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<tr>
<td>Mean Loss</td>
<td>0.15 ± 0.05</td>
<td>5.11 ± 1.38</td>
</tr>
<tr>
<td>(Program 32, dB)</td>
<td></td>
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<tr>
<td>Root Mean Square Fluctuation</td>
<td>1.3 ± 0.1</td>
<td>2.5 ± 0.4</td>
</tr>
<tr>
<td>(Program 32, dB)</td>
<td></td>
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</tr>
<tr>
<td>OPTIC NERVE HEAD</td>
<td></td>
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</tr>
<tr>
<td>Disc Area</td>
<td>1.55 ± 0.08</td>
<td>1.50 ± 0.09</td>
</tr>
<tr>
<td>(mm²)</td>
<td></td>
<td></td>
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<tr>
<td>Disc Rim Area</td>
<td>0.90 ± 0.04</td>
<td>0.78 ± 0.05</td>
</tr>
<tr>
<td>(mm²)</td>
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</table>

Computerized topographic analysis of the optic nerve head was performed using the Rodenstock Analyzer. This instrument has been described in detail and the reproducibility of its measurements and correlation with clinical measurements of the optic disc have been reported. All images were corrected for magnification or minification induced by the optical components of the eye. Measurements of disc area and disc rim area were made and are reported in units of mm². The mean visual field loss was calculated for each visual field by comparison with Octopus age-matched controls. The root mean square fluctuation is reported as a measure of short term fluctuation.

Summary statistics are reported as the mean ± SEM. Statistical analysis was performed using the goodness of fit test and Student’s t-test with a significance level of p < 0.05.

### RESULTS

Ten patients (four males and six females) satisfied the criteria for asymmetric primary open angle glaucoma (APOAG) given above. The visual fields and optic nerves of a typical patient are shown in Figure 1. The control group consisted of twelve eyes of twelve normal patients (five males and seven females). The age (mean ± SEM) of patients in the APOAG group (62.8 ± 1.8 years) was not statistically significantly different from the age of the normal control group (58.9 ± 2.6 years). Data for eyes with normal and abnormal visuals fields in the APOAG group are summarized separately in the Table. There were no statistically significant differences regarding visual acuity, refractive error, intraocular pressure, pupil size, or disc area between the two sets of eyes. Statistically significant differences regarding total visual field loss (p = 0.003) and short term fluctuation (p = 0.012) between the two sets of eyes resulted from the selection criteria. The mean disc rim area in eyes with normal visual fields (0.90 ± 0.04 mm²) was slightly larger than that of eyes with visual field loss (0.78 ± 0.05 mm²); the mean difference between disc rim areas (paired data) was significantly different from 0 (p = 0.008), though this difference was clinically rather small (0.12 mm²). The disc rim area in the normal control group was 1.27 ± 0.09 mm². The disc rim areas of both sets of eyes in the APOAG patients were significantly smaller than in the control group (difference = 0.49 mm² and p = 4×10⁻⁴ for eyes with abnormal visual fields, difference = 0.37 mm² and p = 7×10⁻⁴ for eyes with normal visual fields).
DISCUSSION

Elevated intraocular pressure is an important risk factor for the development of glaucoma. However, less than 1% per year of patients with elevated intraocular pressure and bilaterally normal visual fields develop visual field abnormalities. In patients with asymmetric disease, the development of visual field loss in the previously unaffected eye is much higher, ranging from 25% to 43% after 3-7 years of follow-up. Armaly studied the cup-disc ratio of 52 subjects with unilateral visual field defects from open angle glaucoma. The cup-disc ratios of the unaffected eyes were higher than those of a normal control group; the distribution of cup-disc ratio resembled that of eyes with established glaucomatous visual field loss. Estimates of cup-disc ratio, however, are subjective and may show large intra- and inter-observer differences. There is significant covariation of the cup-disc ratio and disc size, and there is also great variation in values of cup-disc ratio for normal individuals. Measurements of disc rim area may more closely reflect the number of nerve fibers present in the optic nerve. Subjective measurements of disc rim area demonstrate the clinical utility of this approach. Objective, reproducible measurements using computerized image analysis may represent a further refinement of the method.

Quantitative measurements of disc rim area were made using a system of computerized image analysis designed to study the optic nerve head (Rodenstock Analyzer). Asymmetric primary open angle glaucoma (APOAG) patients were selected because of the high likelihood that the visually normal eye will eventually develop perimetric abnormalities, indicating that the eye is an early, "preclinical" stage of glaucoma. The mean optic disc rim area in eyes of the APOAG group with normal visual fields was clinically and statistically significantly smaller than in the control group, and was slightly larger than the contralateral glaucomatous eye. These findings support the hypothesis that early structural abnormalities can be detected in the optic nerve head before visual field defects develop, using contemporary static threshold methods. This conclusion has important implications for the diagnosis and care of glaucoma patients. The examiner's attention should be drawn to the optic nerve in glaucoma suspects, since changes in this structure may precede changes in visual function measured by perimetry. Once visual field abnormalities have become established, visual field measurements may be a more sensitive indicator of progression of glaucomatous optic nerve damage than sequential changes in the optic nerve. Long term, prospective longitudinal studies using quantitative methods to measure and compare the optic nerve and visual field are required to measure the rates of progression of optic nerve damage and visual field abnormalities.

Key words: glaucoma, image analysis, optic disc rim area, optic nerve, perimetry, visual field

RESUMEN

Análisis del aspecto de la papila óptica en pacientes con pérdida unilateral de campo visual asociada a glaucoma de ángulo abierto

En el glaucoma de ángulo abierto incipiente, las anomalías del campo visual pueden ir precedidas de alteraciones de la estructura del nervio óptico. Los autores han estudiado el aspecto del disco óptico de 10 pacientes afectos de glaucoma primario de ángulo abierto, con déficit campimétrico unilateral, y de 12 individuos normales, de edades y sexo similares.

La zona del borde del disco óptico fue medida utilizando un sistema de análisis de imagen computada (Rodenstok Analyzer). En los pacientes con glaucoma primario de ángulo abierto asimétrico, (unilateral) con campo visual normal, el borde de la papila óptica (promedio ± SEM) era discretamente más amplio (0.90 ± 0.04 mm) que en los ojos con alteración del campo visual (0.78 ± 0.05 mm), pero a pesar de ello el borde del disco óptico era inferior (p < 0.0007) al del grupo de control (1.27 ± 0.09 mm).

Estas observaciones apoyan la hipótesis de que la pérdida de tejido propio del borde papilar o de axones de las células ganglionares puede detectarse antes de que se observen alteraciones perimétricas en pacientes afectos de glaucoma primario de ángulo abierto.
**RÉSUMÉ**

Analyse de l’aspect de la papille optique chez les malades qui présentent une perte unilatérale de champ visuel associée à un glaucome à angle ouvert.

Dans le glaucome à angle ouvert précoce, les anomalies du champ visuel peuvent être précédées d’altérations structurelles du nerf optique. Les auteurs ont étudié l’aspect de la papille optique chez 10 malades atteints de glaucome primaire à angle ouvert, avec déficit campimétrique unilatéral, et chez 12 sujets normaux, avec une distribution d’âge et de sexe similaire. L’aire du bord de la papille a été mesurée par un système d’analyse d’image conçu (Rodenstock Analyser). Chez les malades atteints de glaucome primaire à angle ouvert asymétrique (unilatéral) avec champ visuel normal, le bord de la papille optique (moyenne ± SEM) était un peu plus large (0.90 ± 0.04 mm²) que dans les yeux avec altération du champ visuel (0.78 ± 0.05 mm²), mais malgré tout le bord de la papille optique était inférieur (p < 0.0007) à celui du groupe de contrôle (1.27 ± 0.09 mm²).

Ces observations supportent l’hypothèse que la perte de tissu du bord de la papille ou d’axones des cellules ganglionnaires peut être détectée avant que les altérations périmétriques soient évidentes chez les malades atteints de glaucome primaire à angle ouvert.

**SUMMARY**

Image analysis of the optic nerve head in patients with unilateral visual field loss associated with open angle glaucoma

Measurable structural alterations in the optic nerve head may precede visual field abnormalities in early open angle glaucoma. We selected the optic nerve heads of ten patients with unilateral visual field loss from primary open angle glaucoma, and twelve age- and sex-matched normal subjects. Optic disc rim area was measured with a system of computerized image analysis (Rodenstock Analyzer). In patients with asymmetrical (unilobar) primary open angle glaucoma eyes with normal visual fields had a slightly larger (mean ± SEM) disc rim area (0.90 ± 0.04 mm²) than eyes with glaucomatous visual field defects (0.78 ± 0.05 mm²), but had a smaller mean disc rim area (p < 0.0007) than did the control group (1.27 ± 0.09 mm²). These findings support the hypothesis that loss of the optic disc rim or axones of the ganglion cells can be detected before perimetric abnormalities in patients with primary open angle glaucoma.

**REFERENCES**