Patterns of Early Visual Field Loss in Open-Angle Glaucoma

Joseph Caprioli, M.D., Marvin Sears, M.D., and Joseph M. Miller, M.D.

We examined two groups of patients with primary open-angle glaucoma with distinctly different patterns of early visual field loss using two visual field indices: mean defect and loss variance. Patients were selected on the basis of visual field criteria only. Eight patients were selected for diffuse depression of the differential light sensitivity without localized scotomas (mean defect > 3.0 decibels, loss variance < 10.0 decibels). Seven patients were selected for localized scotomas without diffuse depression of the differential light sensitivity (mean defect ≤ 3.0 decibels, loss variance ≥ 20.0 decibels). Patients with diffuse depression manifested intraocular pressures that were higher (mean peak pressure ± S.E.M., 27.6 ± 1.2 mm Hg) than those with localized defects (22.4 ± 1.4 mm Hg). The optic disk rim area of the localized loss group (mean ± S.E.M., 1.02 ± 0.15 mm²) was significantly smaller (P < .05) than the disk rim area of the diffuse loss group (1.33 ± 0.07 mm²). This difference was largely because of thinner temporal disk rims in the localized loss group. Different patterns of visual field loss may be caused by different mechanisms of glaucomatous optic nerve damage.

Patterns of visual field abnormalities in low-tension and high-tension glaucoma have been investigated. Some authors have report-
ed significant differences in patterns of visual field loss between the two groups, while others have found no differences. Variations of patient selection criteria, examination techniques, and differences in stages of the disease and rates of progression make direct comparisons between different studies difficult. More importantly, the single criterion of intraocular pressure (often with infrequent measurements) probably does not adequately separate subpopulations of glaucoma patients. The terms "low tension" and "high tension" imply that intraocular pressure differences alone may adequately separate these two disease entities, but the semantics are not reassuring. Pathogenic definitions are needed to distinguish between different disease processes.

To gain additional useful information in this area, we have identified two groups of patients with open-angle glaucoma using new criteria. We studied the intraocular pressures and optic disks of these groups of patients differentiated on the basis of visual field findings alone. The criteria for visual field abnormalities were designed to separate patients who had only diffuse depression of the visual field from patients whose visual fields had dense, localized scotomas without diffuse depression.

Subjects and Methods

The screening criteria for the initial selection of patients included a diagnosis of primary open-angle or low-tension glaucoma; no history of ocular surgery, disease, or other reason for visual field loss; age 50 to 80 years; refractive error ≤ 3 diopters of ametropia and ≤ 2 diopters of astigmatism; visual acuity ≥ 20/30; total visual field loss of 100 to 300 decibels (Octopus Program 32), root mean square deviation ≤ 3.0 decibels, rate of false negative and false positive ≤ 10%, and pupil size

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From the Glaucoma Service, Department of Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut. This study was supported in part by grants from Research to Prevent Blindness, Inc., the Connecticut Lion's Eye Research Foundation, and Foresight, Inc. Dr. Miller was supported by training grant 5 T32 EY07000-10 from the National Eye Institute.
Reprint requests to Joseph Caprioli, M.D., Yale University School of Medicine, P.O. Box 3333, New Haven, CT 06510-8061.
3.0 mm. These criteria were designed to reduce the likelihood of including eyes with diffuse depression of the visual field caused by nonglaucomatous causes, such as uncorrected refractive error, cataract, miosis, and test inexperience. Patients were selected from the medical records of the glaucoma service, and had more than two automated static threshold visual fields during the last five years. The records were screened by technical staff, while the investigators remained masked to the identity of patients selected. Sixty-three eyes of 59 patients met the initial screening criteria. Of patients who qualified bilaterally, one eye was chosen at random for inclusion in the study. The most recent visual field results of each eye were used for analysis. This group of 59 eyes served as a population from which two subpopulations of eyes with different patterns of field loss were subsequently selected.

Visual field indices introduced by Flamme and associates were used to select eyes with only diffuse visual field loss (without scotomas) and those with only localized dense loss (without diffuse depression). Mean defect is the average loss of differential light sensitivity compared to age-matched normal values of all points tested. Its value is increased little by localized scotomas but increased greatly by diffuse depression of sensitivity. The statistical variance of values of sensitivity loss for all points tested is termed loss variance. This variance includes a component of variance over time (short-term fluctuation). Corrected loss variance is calculated by subtracting short-term fluctuation from loss variance, leaving only the component of spatial variation. Short-term fluctuation can be estimated by measuring the threshold at the same test location multiple times during the examination. Corrected loss variance (and to a lesser extent, loss variance) is a measure of spatial scatter or local nonuniformity of visual field thresholds. It is not affected by uniform diffuse depression of sensitivity, but is increased by localized defects. Thus, mean defect and corrected loss variance are visual field indices sensitive to different types of loss: mean defect is sensitive to diffuse depression, while corrected loss variance is sensitive to localized defects.

Short-term fluctuation can be only approximated using the root mean square deviation of Octopus Program 32, since only ten thresholds are doubly determined. For this reason the loss variance statistic was used, and fields with a root mean square deviation greater than 3.0 decibels were excluded. Mean defect and loss variance were calculated from each visual field after eliminating the most peripheral loci of test locations and the three loci usually containing the blind spot. Arbitrary definitions were made to select patients with predominantly diffuse loss (mean defect > 3.0 decibels, loss variance < 10.0 decibels) and localized scotomas (mean defect ≤ 3.0 decibels, loss variance ≥ 20.0 decibels). Using these definitions, eight eyes were identified with diffuse field loss without scotomas, and seven eyes were identified with localized scotomas and little or no diffuse component.

Information regarding each of the patients whose eyes were selected for final analysis was obtained from our records and from those of referring physicians where appropriate. This included medical history, surgical history, ocular history, ocular medications, blood pressure, and multiple measurements of intraocular pressure. This information was compiled without the investigators' knowledge of the patient's identity, or to which visual field group the patient belonged.

It is impossible to derive a single number that adequately summarizes an eye's intraocular pressure history. Therefore, we took several approaches. The mean, median, high, and low values of all recorded pressures were identified for each eye, on and off medication. The high values invariably occurred at times when no medication was being used. Eyes were also assigned to intraocular pressure categories in a masked fashion as follows: eyes with recorded pressures frequently above 25 mm Hg were included in a high pressure group, eyes with pressures frequently above 20 mm Hg but infrequently above 25 mm Hg were assigned to an intermediate pressure group, and eyes with intraocular pressures infrequently above 20 mm Hg were assigned to a low pressure group.

The optic disk of each patient was analyzed from stereoscopic color photographs taken on the same day the visual field was examined. While viewing a photographic pair stereoscopically, the disk rim was traced on a projected image for each eye and the cup rim marked using contour clues only. Measurements of disk rim area were then made from the tracings using a computerized planimeter. Values were corrected for image magnification or minification using Bengtsson and Krakau's method.
Data were analyzed using Student’s t-test and Fischer’s exact test.

Results

The diffuse loss group contained four men and four women, and the localized loss group contained two men and five women. Two patients in the diffuse group and three patients in the localized group had been treated for systemic hypertension. One patient in the localized group had had an episode of systemic hypotension. All patients in the diffuse group had a clinical diagnosis of primary open-angle glaucoma, while four of the seven patients in the localized group had a diagnosis of low-tension glaucoma. Three patients in the diffuse group and two patients in the localized group had a family history of glaucoma.

There were no statistically significant differences regarding age, visual acuity, refractive error, pupil size, or number of eye medications between the two groups (Table 1). There was no statistically significant difference in the root mean square deviation or total visual field loss between the two groups. There were statistically significant differences between visual field mean defect and loss variance because of the patient selection criteria.

The diffuse group had significantly higher mean, median, and extremes of intraocular pressures than the localized group (Tables 2 and 3). The differences between these intraocular pressure values for the two groups ranged from 3.7 to 5.2 mm Hg. The diffuse group was skewed toward the high range of pressure while the localized group was skewed toward the low range of pressure (Table 3). However, there was some overlap between the two groups.

Quantitative measurements of the disk rim area from stereoscopic photographs of the optic nerve head showed that the rim area was significantly smaller in the localized group compared to the diffuse group. The largest differences were noted in the temporal quadrants of the disk (Table 4). The disk rim has an even width around the entire disk circumference in the diffuse loss group. In the localized loss group, it is thinned temporally (Figs. 1 and 2).

Discussion

Several investigators have searched for differences in patterns of visual field loss in patients with low-tension glaucoma compared to those with high-tension glaucoma. While some have found no differences in types of visual field loss between the two groups, some have found...
others have found significant differences. Variations in selection criteria and technique may explain the apparent discrepancies. Intraocular pressure criteria alone do not seem to adequately subdivide groups of patients. However, if extremes of intraocular pressure are used to divide patients, certain patterns may emerge.

Intraocular pressure levels may not adequately separate potential subgroups of patients with open-angle glaucoma. We developed a new approach to separate subgroups of glaucoma patients without using intraocular pressure measurements. Eyes were assigned to groups solely on the basis of visual field criteria in an effort to study eyes with diffuse visual loss.
field depression contrasted to those with localized scotomas. The selection criteria were designed to minimize the problem created by eyes included in the diffuse loss group because of nonglaucomatous processes, such as cataract, miosis, refractive error, or visual field testing inexperience. Selection criteria also included standards for patient reliability and placed a limit on the magnitude of short-term fluctuation, further reducing the number of eyes eligible. Because few patients met all criteria, the number of subjects in this initial study is small. Nevertheless, different patterns of intraocular pressure and optic nerve cupping did emerge.

Although considerable overlap was evident between the groups regarding intraocular pressure levels, the pressures were consistently higher in the diffuse group compared to the localized group, whether analyzed by intraocular pressure mean, median, high, or low values. A better way of summarizing intraocular pressure history may be to place eyes into intraocular pressure categories in a masked fashion. The diffuse group contained more eyes in the high intraocular pressure category, while the localized group contained more eyes in the low intraocular pressure category. Still, there was some overlap in the intermediate pressure category.

Eyes included in this study were in an early phase of glaucomatous optic nerve damage and were matched for equal amounts of total visual field loss. Eyes with early damage must be studied, since the visual field in advanced or end-stage disease is likely to be similar in all patients. By matching eyes using visual field criteria, it became evident that the pattern of optic disk cupping in patients with localized loss was different from patients with diffuse loss. The diffuse loss eyes had even, symmetrical disk rims that were intact and uniform in thickness. By contrast, eyes in the localized loss group had significant thinning of the disk rim temporally. However, bias may have had an effect on the results. Patients with pressures in the statistically normal range may have been subjected to visual field examinations because of suspicious disk appearances. Patients with normal appearing disks and normal intraocular pressures may not have been tested with visual field examinations. This bias could have contributed to the differences we found regarding intraocular pressure and disk cupping between our groups, but does not explain the existence of different patterns of early visual field loss.

The pathogenic mechanisms responsible for the production of these different patterns requires further study.

We hypothesize, based on this preliminary information, that diffuse loss of visual field sensitivity from glaucoma is largely pressure dependent, and may be secondary to diffuse axonal dysfunction (and later death) leading to progressive concentric enlargement of the optic nerve cup and an evenly distributed thinning of the disk rim. In the localized loss group, visual field loss seems less pressure dependent. Here loss may occur at low as well as at high pressures. The damage to the optic nerve head tends to be less generalized, leading to localized loss of the disk rim temporally. We speculate that pressure-dependent gradual diffuse loss may involve a prolonged phase of ganglion cell dysfunction without death, leading to visual abnormalities with small amounts of progressive cupping. This could explain the presence of psychophysical disturbances preceding detectable morphologic change. Conversely, the localized loss group may be associated with accelerated ganglion cell death leading to thinning of the disk rim and dense scotomas in an early functional phase of the disease. Thus, the rate of ganglion cell death may be an important determinant of the early structural and functional disturbances associated with glaucomatous optic nerve damage.

The eyes selected for this study represent examples of distinct types of visual field loss. Frequently, patients with glaucomatous optic nerve damage have mixed types of visual field loss, with both diffuse depression and localized scotomas occurring in the same field. Diffuse loss may precede scotomas in many patients, and at an advanced stage of the disease, patterns of visual field loss may become indistinguishable. This study represents a new approach to identify possible subsets of patients with glaucoma and to quantify the abnormalities within these subsets.

References

2. Caprioli, J., and Spaeth, G. L.: Comparison of


