Achromatic and Short-Wavelength Automated Perimetry in Patients With Glaucomatous Large Cups

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Objective: To evaluate visual function and optic disc features in patients with large cup-disc ratios (C/Ds).

Methods: One eye of 86 patients with vertical C/Ds by contour of at least 0.8, who had undergone both standard achromatic automated perimetry (SAP) and short-wavelength automated perimetry (SWAP) testing, was selected retrospectively. Two masked glaucoma specialists independently graded stereoscopic photographs for vertical C/Ds, rim thinning, notching, excavation, optic disc hemorrhages, and nerve fiber layer defects. Visual fields were classified as abnormal if the glaucoma hemifield test result, corrected pattern standard deviation, or mean deviation was outside age-specific normal limits. Confocal scanning laser ophthalmoscopy was used to determine disc area.

Results: SAP and SWAP results were abnormal in 44 (51%) and 52 (60%) of 86 patients, respectively. In patients with normal SAP results, SWAP results were abnormal in 14 (33%) of 42 patients. In patients with normal SWAP results, SAP results were abnormal in 6 (18%) of 34 patients. Small discs are associated with an abnormal SAP result \((P = .01)\) and an abnormal SWAP result \((P = .09)\). An increased vertical C/D greater than the qualifying level of 0.8 was associated with an abnormal SAP or SWAP result \((P = .001)\). Rim thinning \((P = .01)\) and disc hemorrhages \((P = .04)\) were associated with an abnormal SAP result.

Conclusions: Many patients with large C/Ds have normal SAP and SWAP results. Compared with SAP, SWAP results were abnormal in a higher percentage of these patients. If a patient has a large C/D and normal SAP results, SWAP testing may detect functional loss earlier. If glaucoma is defined by both structural and functional loss, patients with large vertical C/Ds, normal SAP results, and abnormal SWAP results may have glaucoma. Longitudinal studies are needed to assess this hypothesis and determine whether these patients subsequently develop abnormal SAP results as well.


CURRENTLY, glaucoma is diagnosed with observation of both structural changes in the appearance of the optic disc and functional visual field loss with standard achromatic automated perimetry (SAP). With either structural or functional changes alone, patients often are considered to be glaucoma suspects and are followed up with appropriate serial testing and treatment. Some of these individuals have a higher risk of developing glaucoma and subsequently will have progressive changes in the appearance of the optic disc or visual field.

One group of patients that has been described as being at particularly high risk for developing glaucoma is individuals with large cup-disc ratios (C/Ds).\(^1\) Hart et al\(^1\) and Yablonski et al\(^3\) found that a large C/D was the best predictor of subsequent visual field loss in patients suspected of having glaucoma. Johnson et al\(^1\) found vertical C/Ds to be significantly associated with short-wavelength automated perimetry (SWAP) deficits. However, Tielsch et al\(^5\) suggested that C/D is a poor predictor of subsequent visual field loss.

Recently, several techniques for diagnosing functional and structural loss due to glaucoma have been developed. One of them, SWAP, has been demonstrated to detect subsequent visual field loss in patients with ocular hypertension as much as 3 years earlier than SAP.\(^6\) The purpose of the present study was to evaluate visual function with SAP and SWAP and optic disc features in patients with large C/Ds.

RESULTS

SAP and SWAP

The results of SAP and SWAP were abnormal in 44 (51%) and 52 (60%) of 86 patients, respectively. In patients with
SUBJECTS AND METHODS

SUBJECTS

Subjects were retrospectively selected from the research database of the Glaucoma Center at the University of California, San Diego. This study was approved by the Human Subjects Committee of the University of California, San Diego, and informed consent was obtained from each subject. One eye of 201 patients had vertical C/Ds by contour of greater than or equal to 0.8 on stereoscopic photographs. A subgroup of 101 had undergone at least 2 SAP and SWAP evaluations. Fifteen patients were excluded because of general reduction of sensitivity with either SAP or SWAP. This resulted in 86 patients available for analysis.

There were 32 men and 54 women. Their mean (±SD) age was 65.4 ± 10.7 years (range, 40-85 years). Exclusion criteria included poor-quality stereoscopic photographs, presence of significant ocular disease other than cataract, unreliable visual fields (false responses or fixation losses >25%), patients with myopia greater than 5 diopters, and use of medications that affect color vision. If general reduction of sensitivity (overall sensitivity of the visual field depressed outside 99.5% of age-specific norms) was present on the glaucoma hemifield test print-out, these patients were excluded to minimize possible cataract effects.

OPTIC DISC PHOTOGRAPHY

Simultaneous stereoscopic photographs (Topcon Simultaneous Stereo Camera TRC-5S; Topcon Instrument Corporation of America, Paramus, NJ) had been obtained for all patients and reviewed with a simultaneous stereoscopic viewer (Yashika, Inc, US Centrax Distributor, Paramus, NJ) under uniform fluorescent lighting conditions. All photographs were of good quality. Because the consistency of clinical C/D estimates is poor even among glaucoma experts, all photographs were required to have similar grading of vertical C/Ds by 2 different glaucoma specialists. The C/D was graded to the nearest 0.1, which resulted in 3 possible outcomes: 0.8, 0.9, or 1.0. Photographs were reviewed in a masked fashion while grading other disc photographs from both healthy and glaucomatous patients. If 1 reviewer graded the vertical C/D to be less than 0.8, the subject was excluded from the analysis. In addition to the C/D, the photographs were examined for excavation, nerve fiber layer defects, notching, rim thinning, and optic disc hemorrhage. Excavation was defined as undermining of the neuroretinal rim. A focal nerve fiber layer defect was described when its width, 1 disc diameter from the disc margin, was larger than a major retinal vein and it diverged in a wedge or arcuate shape. Notching was considered to be focal rim thinning less than 2 clock hours (60°). Rim thinning was defined as neuroretinal rim narrowing present for more than 2 clock hours. The photographs were classified as nonglaucomatous, suspicious, or glaucomatous using a masked, forced-choice design. Photography was performed on a separate day before visual field testing. The mean (±SD) time was 10.6 ± 10.5 months before SWAP testing.

VISUAL FIELDS

Procedures for SAP and SWAP were similar; we used Humphrey visual field program 24-2 full-threshold algorithms. To minimize the possibility of a learning effect, patients were included only if they had previously undergone at least 2 prior visual field examinations and their false responses and fixation losses were less than 25%. Patients were defined as having abnormal fields if there was repeatable corrected pattern standard deviation outside the 95% limits, glaucoma hemifield test result outside 99.5% of age-specific norms (outside normal limits on Statpac2 for SAP or our age-specific norms for SWAP [n = 214]), or mean deviation outside the 95% limits without general reduction in sensitivity. SWAP testing was completed within 1 month before or 3 months after the SAP testing. In 69 patients, it was completed on the same day. All visual field loss was confirmed on a consecutive test. Mean (±SD) period between confirmatory visual fields for SAP and SWAP was 10.8 ± 7.4 and 15.1 ± 7.8 months, respectively.

DISC AREA

Because C/D is related to disc size, the relationship of these factors was compared with disc area. Disc area was assessed using confocal scanning laser ophthalmoscopy (Heidelberg Retina Tomograph, version 2.01; Heidelberg Engineering, Heidelberg, Germany) in 79 of 86 patients. In the other 7 patients, confocal scanning laser ophthalmoscopy was not done. The margin of the disc on the topographic image was outlined by a trained technician masked to the purpose of the study and disc area computed. These values were corrected for magnification using keratometry readings.

RISK FACTORS

Risk factors for glaucoma, including highest intraocular pressure (IOP), secondary glaucoma (pigmentary dispersion [n = 6], pseudoxfoliation [n = 6], and chronic angle closure [n = 2]), African American race, family history of glaucoma in a primary relative, older age, and presence of hypertension, vascular disease, vasospasm, or migraine, were assessed in each patient. The highest IOP was the highest IOP measurement obtained while the patient was not taking medication, excluding measurements that may have been taken during a postoperative visit. All IOP measurements were obtained with Goldmann tonometry.

STATISTICAL ANALYSIS

Differences in mean values between the 2 groups for continuous variables, such as IOP, age, and disc area or discrete outcomes such as C/D, were analyzed using an unpaired 2 test. For proportions such as the presence of risk factors, male sex, and optic disc appearance, statistical significance was determined using the χ2 test. For multiple comparisons, a Bonferroni correction was used. A level of significance was determined at a P value equal to .003 (0.05/16) for demographic characteristics and .003 (0.05/16) for disc characteristics. The power to detect a difference was determined for all nonsignificant comparisons.
normal SAP results, SWAP results were abnormal in 14 (33%) of 42. In patients with normal SAP results, SAP results were abnormal in 6 (18%) of 34. Of 86 patients, 38 (44%) had abnormal results on both SAP and SWAP; 28 (33%) had normal results on both SAP and SWAP; 14 (16%) had abnormal results only on SWAP; and 6 (7%) had abnormal results only on SAP.

**RISK FACTORS**

There was no significant difference in age between patients with normal or abnormal SAP results (Table 1) and normal or abnormal SWAP results (Table 2). The highest recorded IOP (mean ± SD) of patients was 25.4 ± 6.3 mm Hg. There was no significant difference between the highest recorded IOP in patients with abnormal or normal SAP results (Table 1) and abnormal or normal SWAP results (Table 2).

There was no significant difference in the number of patients of African American race or with secondary glaucoma, family history of glaucoma, diabetes, migraine, or coronary artery disease and/or vascular disease between patients with a normal or abnormal SAP result (Table 1) or a normal or abnormal SWAP result (Table 2). The power to detect a difference in demographic or risk factors was less than 0.25 in all analyses. Given the small expected differences in the prevalence of risk factors, the sample sizes were not adequate to detect a significant difference.

**OPTIC DISC ANALYSIS**

The vertical C/D (mean ± SD) was 0.85 ± 0.05. Larger mean vertical C/D above the qualifying level of 0.8 was significantly associated with abnormal SAP (Table 3) and SWAP (Table 4) results (P = .001). In addition, the percentage of patients with rim thinning (P = .01) or disc hemorrhages (P = .04) tended to be larger in the subjects with abnormal SAP results than those with normal SAP results, although this finding was not statistically different after Bonferroni correction.

**DISC AREA**

The disc area (mean ± SD) was 2.19 ± 0.60 mm². Patients with a smaller disc area tended to have an abnor-
Our results indicated that in patients with vertical C/Ds of at least 0.8, the presence of abnormal SAP results (51%) or abnormal SWAP results (60%) was relatively common. Approximately two thirds (67%) of the subjects had abnormal results on at least one type of testing. In patients with normal SAP results, an abnormal SWAP result occurred in 33.3%. This group is of particular interest because visual field loss would not be observed if tested only with SAP. Our findings are in agreement with those of Johnson et al. In their study, the prevalence of SWAP abnormalities in patients with ocular hypertension (approximately 18 eyes) and normal SAP results and C/Ds of 0.8 and 0.9 was approximately 43% and 25%, respectively.

In the present study, among patients with a vertical C/D of at least 0.8, 33% had both normal SAP and SWAP results. Several alternative explanations may account for this finding.

First, some of these eyes may be healthy and will not develop glaucoma even during lengthy observation. Jonas et al. identified certain features to differentiate glaucomatous optic discs. Some of the features ascribed to glaucomatous optic discs were presence of beta zone of parapapillary atrophy, abnormal rim configuration, thin vessel caliber, and absence of a cilioscleral vessel. These characteristics were not evaluated in this study.

In glaucoma, functional damage often evolves only after structural changes have already occurred at the optic disc. Therefore, a second possibility is that some of these eyes have glaucomatous optic neuropathy with a glaucomatous optic disc but have not yet developed visual field abnormalities. Some of these patients might subsequently develop glaucomatous visual field defects detected by SAP. Peigne et al. and Tomita et al. reported that patients with glaucomatous optic discs and normal standard visual fields had intermediate amounts of nerve fiber layer thickness, nerve fiber defects, pallor, and fluorescein angiographic defects compared with healthy and glaucomatous patients. Hart et al. reported vertical C/D to have the greatest significance for predicting visual field loss in patients with ocular hypertension with initially normal standard visual fields. In addition, Yablonski et al. reported that patients suspected of having glaucoma with vertical C/Ds of greater than 0.6 or greater than 0.8 developed glaucomatous visual field loss over 5 years with Goldmann perimetry in 36.6% and 83.3%, respectively.

Other factors also might contribute to the absence of visual field loss in these patients with both normal SAP and SWAP results and C/Ds of at least 0.8. In the patients with normal SAP results, 69% were taking treatment to lower IOP. Possibly, in this susceptible group of patients, treatment had been successful in preventing visual loss. Few of our subjects were African Americans (n = 3) or had secondary glaucomas (n = 6). These risk factors have been associated with progression to glaucoma, and their absence suggests the possibility of a less susceptible patient population with a slowly advancing disease. The population from which this sample was drawn included few African Americans; therefore, application of these data to populations with a greater percentage of African Americans may not be warranted.

A third possibility is that glaucomatous functional loss already is present in some of these eyes but is not detected by our use of SAP and SWAP. These patients may have had early selective damage of functional pathways not detected by SWAP, and other tests such as motion automated perimetry and frequency doubling perimetry might detect abnormalities in some of these patients. The presence of diffuse visual field loss also might not have been detected in our study. Although diffuse visual field loss as an early sign of glaucoma has been questioned, patients with neuroretinal rim thinning may have generalized decreased sensitivity that would not be detected with focal measures such as glaucoma hemifield test and corrected pattern standard deviation, which were evaluated in this study. In this regard, we also eliminated patients with generalized reduction of sensitivity (n = 15) to minimize possible cataract effects.

In our study, an increased vertical C/D above the qualifying level of 0.8 (P ≤ .001) was associated with abnormal SAP and SWAP results. This is consistent with earlier studies that showed a large C/D was an important risk factor for glaucomatous visual field loss. Other optic disc features in this study associated with abnormal SAP or SWAP results included smaller disc area, rim thinning, and presence of nerve fiber layer defects. There were no demographic or risk factors associated with abnormal SAP or SWAP results.

The relationship of optic disc area and susceptibility to glaucoma is interesting and controversial. Some investigators have suggested that a larger optic disc is more likely to develop glaucomatous damage. Others have suggested that disc size is unrelated to glaucoma susceptibility. In this study, patients with smaller disc areas and large C/Ds had a greater likelihood of functional visual loss, although this finding was not statistically significant after Bonferroni correction. This may be explained by a larger ratio of the number of nerve fibers per neuroretinal rim area in a smaller optic disc as the result of a smaller scleral canal. Therefore, a larger decrease in the number of optic nerve fibers would be expected before the C/D would enlarge. Eyes with smaller disc areas would therefore have more extensive disease at a given C/D.

Compared with SAP, SWAP results were abnormal in a higher percentage of patients with large C/Ds. If a patient has a large C/D and normal SAP result, SWAP testing may detect functional loss earlier. If glaucoma is defined by both structural and functional loss, patients with large vertical C/Ds and normal SAP but abnormal SWAP results may have glaucoma. Longitudinal studies are needed to assess this hypothesis and determine whether these patients subsequently develop abnormal SAP results as well.

Accepted for publication March 30, 1999.

This study was supported by grants EY08208 (Dr Sample), EY11008 (Dr Zangwill), and EY11158 (Dr Weinreb) from the National Eye Institute, Bethesda, Md.
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REFERENCES


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