Classification of Visual Field Abnormalities in the Ocular Hypertension Treatment Study

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Objectives: (1) To develop a classification system for visual field (VF) abnormalities, (2) to determine interreader and test-retest agreement, and (3) to determine the frequency of various VF defects in the Ocular Hypertension Treatment Study.

Methods: Follow-up VFs are performed every 6 months and are monitored for abnormality, indicated by a glaucoma hemifield test result or a corrected pattern SD outside the normal limits. As of January 1, 2002, 1636 patients had 2509 abnormal VFs. Three readers independently classified each hemifield using a classification system developed at the VF reading center. A subset (50%) of the abnormal VFs was reread to evaluate test-retest reader agreement. A mean deviation was calculated separately for the hemifields as an index to the severity of VF loss.

Main Outcome Measures: A 97% interreader hemifield agreement.

Results: The average hemifield classification agreement (between any 2 of 3 readers) for 5018 hemifields was 97% and 88% for the 1266 abnormal VFs that were reread (agreement between the first and second classifications). Glaucomatous patterns of loss (partial arcuate, paracentral, and nasal step defects) composed the majority of VF defects.

Conclusion: The Ocular Hypertension Treatment Study classification system has high reproducibility and provides a possible nomenclature for characterizing VF defects.

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the frequency, location, and shape of initial glaucomatous visual field deficits. By using inclusion/exclusion criteria that restrict the study sample to individuals with small, shallow visual field deficits, some investigations have assumed that these visual field defects represent early glaucomatous visual field loss.

Unlike other studies, the OHTS provides a unique opportunity to examine the characteristics of initial glaucomatous visual field loss in a longitudinal study. There are many reports that use quantitative methods for describing progressive visual field loss. However, quantitative methods may not capture information on the pattern and location of visual field loss that may be more helpful in tracking the progression of glaucoma.

To be eligible for the OHTS, each eye was required to have 2 sets of normal and reliable visual fields at entry in addition to other eye-specific and patient-specific eligibility criteria. Follow-up visual fields were then obtained at 6-month intervals. The purpose of this report was to characterize visual field defects in OHTS participants observed during follow-up. To accomplish this, it was necessary to develop a classification system and to use trained readers to perform these classifications with high interreader agreement (agreement between readers for a given reading) and high test-retest reader agreement (agreement between the first and second reading).

METHODS

The procedures employed by the OHTS and the baseline characteristics of OHTS participants have been previously described. Briefly, 1636 participants were randomized in the OHTS at 22 participating clinical centers. To be eligible for the OHTS, participants were required to have an intraocular pressure between 24 and 32 mm Hg in one eye and between 21 and 32 mm Hg in the fellow eye. Visual fields were performed using Humphrey (Carl Zeiss Meditech, Dublin, Calif) 30-2 full-threshold, white-on-white, static perimetry. To meet visual field eligibility criteria, individuals completed a minimum of 2 and a maximum of 3 visual field tests. Two of the 3 tests had to meet reliability criteria of less than 33% false positives, less than 33% false negatives, and less than 33% fixation losses. Two of the 3 visual fields had to be judged normal by the visual field reading center, requiring a STATPAC II (Carl Zeiss Meditech) global indices of corrected pattern SD (CPSD) within the 95% age-specific population norm, and a glaucoma hemifield test result within the 97% age-specific population norm. The fields had to be normal and reliable in both eyes on 2 examinations as determined by the visual field reading center, and the optic nerve heads had to be normal in both eyes on clinical examination and in stereoscopic optic disc photographs as determined by the optic disc reading center. Follow-up visual field examinations were performed at 6-month intervals.

According to the OHTS protocol, an abnormal visual field (abnormal from any cause) is defined as having a glaucoma hemifield test outside normal limits and/or a CPSD with P<.05. In addition to the OHTS criteria for an abnormal visual field during follow-up, a secondary definition for the abnormality of each hemifield was created by the visual field reading center to describe the type and extent of the visual field defect. According to OHTS criteria, one hemifield could be abnormal and the other could be normal but still contain abnormal points. The secondary definition of abnormality is defined as: (1) having a single point that is worse than the .05 probability level on the total and/or pattern deviation plots; (2) 3 adjacent points (cluster) beyond normal limits (P<.05) and at least 1 point worse than the .01 probability level on the total and/or pattern deviation plots (a cluster is defined as ≥2 horizontally or vertically contiguous abnormal points with P<.05); and (3) 3 or more clustered points worse than the .05 probability level on the total and/or pattern deviation plot. For all 3 classification evaluations, the pattern of loss has to be consistent with ocular visual field abnormalities. Thus, for a hemifield to be classified as normal, it must not meet any of the aforementioned criteria for hemifield abnormality.

The procedures for hemifield classification are as follows: (1) The superior and inferior hemifields of visual fields that meet the OHTS abnormality criteria are evaluated separately, with the superior hemifield being classified first. Hemifield classifications are separated by a slash. If a defect straddles the horizontal midline, only a single designation is given and no slash is presented. (2) In general, the pattern on the deviation plot ("total" or "pattern") showing the greater number of abnormal points is used to determine the appropriate classification for a hemifield abnormality. However, the other deviation plot as well as the gray scale are evaluated to confirm the appropriateness of the classification. Abnormal points that are extraneous to the salient pattern are considered less important for the determination of the hemifield classification. Thus, the most predominant pattern is classified.

Between February 28, 1994, and January 1, 2002, 38328 follow-up visual fields were evaluated in this report, which included 2509 that met the OHTS criteria for abnormality (glaucomatous and nonglaucomatous; reproducible and not reproducible). Hemifields were not evaluated for the secondary definition of abnormality unless the visual field first met the OHTS criteria for abnormality. Approximately 94% (2345/2509) of the abnormal visual fields classified in this report were reliable, and only 6% (164/2509) were unreliable.

In 1990, 2 of us (J.L.K. and C.A.J.) began characterizing the types and severity of visual field defects in the Optic Neuropathy Treatment Trial (ONTT). As with ONTT, the authors developed a classification system for the OHTS in 1997 to identify glaucomatous visual field abnormalities in patients with ocular hypertension. The categories included patterns of visual field loss that were characteristic of glaucoma, patterns that were characteristic of other ocular and neurologic diseases, and patterns that were associated with testing artifacts. In the developmental stages of the classification system, each of the readers evaluated a subset of 129 abnormal visual fields. These fields were subsequently included in the final set of the 2509 abnormal fields. Each reader’s classification from this training set was compared and discussed to refine and standardize the criteria for developing the 17 mutually exclusive categories presented in Table 1. Once a true collaboration of visual field classifications was established for the subset, the 2 experienced readers trained a third visual field reader. To become a certified visual field reader, one must be able to earn a score of 80% or better on (1) 10 questions related to the OHTS visual field classifications system and (2) a set of 200 previously classified abnormal fields. If the required score is not obtained on either test on the first try, a second set of 10 questions and a second set of 200 abnormal visual fields are given. Since the visual field reading center is masked to the participant’s diagnosis, optic disc characteristics, and randomization assignment, the classification of the visual field deficit is strictly based on the pattern of visual field abnormality.

Following the training set, 2509 abnormal visual fields were selected by querying the visual field reading center dataset for visual fields that met the OHTS criteria for abnormality (abnormal glaucoma hemifield test and/or CPSD with P<.05). Each of the readers classified the entire group of 2509 abnormal visual fields in groups of approximately 100. The hemifields were
readers. If at least 2 readers agreed with an abnormality classification, the majority classification was accepted (2 of 3 readers in agreement). If all 3 readers disagreed, then the visual fields were adjudicated by group consensus to reach a final classification of the hemifield abnormality. We report agreement between readers prior to adjudication.

The test-retest reader agreement of hemifield classifications was determined by rereading a 50% sample (1266/2509) of the abnormal visual fields. The sample reflected the distribution of the 17 abnormality classifications in the first reading. Agreement between the final classifications in the first reading and the final classifications in the second reading was determined. The final classification was used to determine agreement between the first and second readings of the same visual field. The final classification could be the classification determined by the unanimous agreement among the 3 readers, the majority of the 3 readers (2 of 3 readers), or by consensus when there was no initial agreement between the readers.

Examples of visual field abnormality classifications are presented in Figure 1 (nerve fiber bundle pattern likely to be due to glaucoma), Figure 2 (other patterns of visual field loss likely to be due to ocular or neurologic abnormalities other than glaucoma), and Figure 3 (visual field loss probably due to testing artifacts). For illustrative purposes, more than one example-
ample is shown to demonstrate the variation in severity for some classification categories.

To determine the extent of visual field loss associated with each of the visual field classifications, we calculated the mean deviation (MD) separately for the superior and inferior hemifields. This was accomplished by modifying a statistical analysis package previously developed for other purposes and referred to as Statpac-like Analysis for Glaucoma Evaluation. The analysis package was based on visual field data obtained from 348 normal control subjects between the ages of 18 and 85 years. The data were obtained from 5 North American sites (University of California–Davis, Sacramento; University of Cali-

Figure 1. Examples of nerve fiber bundle abnormalities in the Ocular Hypertension Treatment Study, classified by total or pattern deviation plots. More than one example may be shown to demonstrate the variation in severity. The arrow indicates the classified abnormal hemifield.
This normative dataset served as the basis for deriving a Microsoft Excel macro program similar to Statpac that calculates visual field indices as well as total and pattern deviation probability values. The program was modified to provide separate MD values for the superior and inferior hemifields.

RESULTS

Figure 4 shows the number and frequency of final classifications for the 5018 hemifields in the OHTS. Based strictly on the pattern of visual field loss, 57.7% (2893/5018) of the hemifields were judged to be typically glaucomatous, and 20.3% (1017/5018) were judged to be typically nonglaucomatous (possibly owing to other ocular abnormalities and/or testing artifacts). The most frequent hemifield classifications were those likely to be associated with glaucoma, including partial arcuate, paracentral, and nasotemporal step defects. A total of 11.5% of the hemifield classifications were possibly associated with other ocular or neurologic abnormalities, such as widespread, central, and total loss, partial hemianopia, vertical step, and quadrant defects. A total of 8.8% of the hemifield classifications were likely to be associated with testing artifacts, such as partial peripheral rim, superior depression, inferior depression, and peripheral rim defects. Hemifields exhibiting advanced visual field loss were also classified. A total of 7.6% of the hemifield classifications included patterns indicative of advanced glaucomatous abnormalities.

Table 2 presents the interreader agreement for 5018 hemifields using our classification system prior to adjudication, with agreement between any 2 of the 3 possible readers at 97% for superior hemifields, and 97% for inferior hemifields. All 3 readers were in complete agreement on 66% of the superior hemifields and on 64% of the inferior hemifields.

Figure 2. Examples of ocular or neurologic abnormalities in the Ocular Hypertension Treatment Study, other than glaucoma, classified by total or pattern deviation plots. More than one example may be shown to demonstrate the variation in severity. The arrow indicates the classified abnormal hemifield.
To evaluate the agreement (2 of 3 readers) of visual field classifications, 50% (1266/2509) of the total number of abnormal visual fields were evaluated a second time. Table 3 presents the hemifield classification agreement, with the final classification following adjudication, as 88% for superior hemifields and 89% for inferior hemifields. 

Table 3. Interreader Agreement of 3 Readers

<table>
<thead>
<tr>
<th>Hemifield</th>
<th>No. of Readers in Agreement (Prior to Adjudication)</th>
<th>No. of VFs</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior</td>
<td>3</td>
<td>1647</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>788</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>74</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2509</td>
<td>100</td>
</tr>
<tr>
<td>Inferior</td>
<td>3</td>
<td>1616</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>818</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>75</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2509</td>
<td>100</td>
</tr>
</tbody>
</table>

Abbreviation: VF, visual field.

Table 3. Test-Retest Agreement Between Final Classifications

<table>
<thead>
<tr>
<th>Hemifield</th>
<th>No. of Readers in Agreement With Final Classification (Following Adjudication)</th>
<th>No. of VFs</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior</td>
<td>3</td>
<td>883</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>231</td>
<td>18</td>
</tr>
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<td>1</td>
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<td></td>
<td>0</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1266</td>
<td>100</td>
</tr>
<tr>
<td>Inferior</td>
<td>3</td>
<td>894</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>226</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>120</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1266</td>
<td>100</td>
</tr>
</tbody>
</table>

Abbreviation: VF, visual field.

Figure 3. Examples of probable artifact abnormalities in the Ocular Hypertension Treatment Study classified by total or pattern deviation plots. More than one example may be shown to demonstrate the variation in severity. The arrow indicates the classified abnormal hemifield.

Figure 4. Pie chart of the frequency distribution of hemifield abnormality classifications following adjudication.

Figure 5. Box and whisker plot of the mean deviation values of the Ocular Hypertension Treatment Study combined hemifield abnormalities following final adjudication (mean/10th, 25th, 75th, and 90th percentiles). (Note: No hemianopic defects are shown here since there were none classified.)
Automated perimetry has become an accepted standard of practice, allowing physicians to monitor the development of glaucomatous visual field loss. Very few longitudinal studies of any size and magnitude involving the classification of abnormal glaucomatous visual fields have been conducted.

Previous investigators have developed classification systems to identify the pattern and severity of glaucomatous visual field loss. In general, they have looked at the pattern of visual field loss in a cross-sectional fashion, which has been used to predict future progressive glaucomatous visual field changes.

Recent glaucoma trials, such as the Glaucoma Laser Trial, Normal Tension Glaucoma Collaborative Study, Advanced Glaucoma Intervention Study, Collaborative Initial Glaucoma Treatment Study, and Early Manifest Glaucoma Trial, developed visual field analysis systems to determine if change and progression had taken place. Of these trials, none that used automated perimetric techniques attempted to classify the visual fields on a systematic basis to characterize the pattern, frequency, location, and shape of the initial glaucomatous field defects. To our knowledge, the OHTS is the first prospective, longitudinal study to examine the characteristics of the earliest glaucomatous field changes in a large group of participants with ocular hypertension. At baseline, all OHTS participants were required to have 2 sets of normal and reliable visual fields for each eye. In contrast with many of the previous glaucoma trials, a strict quality control system was developed to emphasize reliable visual field information using modern automated perimetric techniques. The OHTS participants have been studied longitudinally for more than 7 years, with a total of 38,328 follow-up visual field evaluations performed thus far, using the classification system described in this report.

Our findings indicate that a classification system for characterizing the pattern and extent of glaucomatous and other visual field abnormalities can be implemented with high system agreement and high system reproducibility when used by trained visual field readers. We have previously developed a similar visual field classification system for characterizing deficits associated with optic neuritis as part of the Optic Neuritis Treatment Trial. More than 10 years of experience, the 2 visual field readers have created strict criteria for certification (a score ≥80% or better on 10 questions related to the OHTS visual field classifications system and on a set of 200 previously classified abnormal fields) and have successfully trained a third reader. A fourth visual field reader is currently being trained as a “back-up” reader. It is possible to obtain a high degree of consistency in classifying visual fields with this system when a criterion of agreement by 2 of 3 readers is employed. We obtained an average reader agreement of 97% for all hemifield classifications (Table 2); system reproducibility was also found to be very good at 88% for superior hemifield agreement and 89% for inferior hemifield agreement (Table 3).

There are current limitations in using this classification system. This system has not been evaluated using the 24-2 standard test pattern or the Swedish Interactive Testing Algorithm test patterns. The sample of visual field abnormalities detected in the OHTS at this time contains few visual fields with advanced glaucomatous changes. Only 7.6% (381/5018) of the hemifields show advanced glaucomatous visual field loss. Nevertheless, given these limitations, the principles could apply with our classification definitions and procedures in classifying future patterns of visual field changes while using various testing parameters.

The most common classifications observed in this report were those likely to be associated with early glaucomatous damage, such as partial arcuate (21.7%), paracentral (15.6%), and nasal step (10.6%) defects (Figure 4). Although the frequency and type of glaucomatous defects have been previously reported by other studies, they have been based on cross-sectional data obtained from participants with existing visual field loss. Since the OHTS participants began the study with normal visual fields and were followed up longitudinally at 6-month intervals, the results from this study clearly represent early glaucomatous visual field loss.

A number of visual field abnormalities are related to other medical conditions, such as partial hemianopsia (0.8%) and quadrant (0.1%) defects. Altitudinal defects (0.7%) could be related to glaucoma, anterior ischemic optic neuropathy, or other optic neuropathies. Additional visual field abnormalities, such as central loss (1.2%) and diffuse widespread loss (7.8%) could be related to macular degeneration and cataracts, respectively, or other retinal abnormality. The paracentral scotoma (15.6%) is a common abnormality and could represent early glaucoma, noise in the testing system, or other abnormalities (Figure 4).

Approximately 9% (437/5018) of the total number of hemifields examined in this report were likely to be associated with testing artifacts: superior depression and inferior depression (2.9%) and partial and total peripheral rim (5.9%) (Figure 4). This represents only 0.6% (437/76565) of the total number of hemifields (as of January 1, 2002) associated with testing artifacts, signifying a remarkably low percentage of artifactual test results in OHTS follow-up visual fields. We have previously reported that reliability indices (false positives, false negatives, and fixation losses) have also been very low for the OHTS, with an unreliability rate of only 3%. Our current findings are consistent with the prior results and suggest that the use of a standardized protocol, training and certification of technicians, and ongoing quality control assessment of all visual fields make it possible to obtain quality visual field data with low unreliability rates.

The OHTS outcome information can be found in recently published articles by Kass et al and Gordon et al that report whether topical ocular hypotensive medication delays or prevents the onset of POAG and what baseline factors predict the onset of POAG in the OHTS. The present report serves as a baseline for the OHTS classification system. Now that the OHTS findings have become available, we will begin to analyze these data.

The classification system that we have developed for the OHTS has been used to characterize the pattern and extent of visual field defects observed in visual fields clas-

References 8-10, 12, 14, 15, 18, 19, 25, 34.
sified as abnormal according to the study protocol. It is important to remember that not all abnormal visual fields in this article reflect visual field defects attributable to glaucoma; they only demonstrate patterns of visual field loss. Future articles will examine this relationship. The most current sample of abnormal hemifields in OHTS predominately reflects early damage, since only 7.6% of the hemifields reflected advanced damage. Further follow-up will define the classifications for advanced glaucomatous visual field loss. As the OHTS continues, we will report longitudinal glaucomatous changes and determine the pattern of progressive visual field loss. The ability of this classification system to provide alternative methods of tracking visual field progression is yet to be determined and will be evaluated in future reports.

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forms). Third, potential study subjects with significant opacification of the anterior chamber or without light perception were excluded from the EVS. Because these eyes with more severe infection or involving more virulent organisms were excluded from the EVS, the effect might have shifted the EVS outcomes to more favorable results. Although the EVS provides general guidelines, the clinician ultimately must decide on the best treatment strategy for the individual patient.

In summary, the EVS has had a significant effect on the management of patients with acute-onset endophthalmitis following cataract surgery and secondary intraocular lens implantation, as well as on the cost associated with management of this disease. Most patients are treated in an office setting with vitreous tap and intravitreal antibiotic injection rather than in the operating room with pars plana vitrectomy, and most are managed as outpatients without intravenous administration of antibiotics.

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REFERENCES


Correction

Error in “Methods” Section. In the Clinical Sciences article titled “Classification of Visual Field Abnormalities in the Ocular Hypertension Treatment Study,” published in the May 2003 issue of the Archives (2003;121[5]:643-650), on page 644, second column, line 1, the incorrect published statement reads “(2) 3 adjacent points (cluster) beyond normal limits (P<.05) and at least 1 point worse than the .01 probability level on the total and/or pattern deviation plots (a cluster is defined as ≥2 horizontally or vertically contiguous abnormal points with P<.03); and. . . ” The statement should read “(2) 2 adjacent points (cluster) beyond normal limits (P<.05) and at least 1 point worse than the .01 probability level on the total and/or pattern deviation plots (a cluster is defined as ≥2 horizontally or vertically contiguous abnormal points with P<.05) and. . . ”