Bilateral Sequential Nonarteritic Anterior Ischemic Optic Neuropathy

A Comparison of Visual Outcomes in Fellow Eyes Using Quantitative Analysis of Goldmann Visual Fields

Jennifer Loh Mercado, MD; Valerie A. Purvin, MD; Aki Kawasaki, MD; Darrell WuDunn, MD, PhD

**Objective:** To better define the concordance of visual loss in patients with nonarteritic anterior ischemic optic neuropathy (NAION).

**Methods:** The medical records of 86 patients with bilateral sequential NAION were reviewed retrospectively, and visual function was assessed using visual acuity, Goldmann visual fields, color vision, and relative afferent papillary defect. A quantitative total visual field score and score per quadrant were analyzed for each eye using the numerical Goldmann visual field scoring method.

**Results:** Outcome measures were visual acuity, visual field, color vision, and relative afferent papillary defect. A statistically significant correlation was found between fellow eyes for multiple parameters, including logMAR visual acuity (P = .01), global visual field (P < .001), superior visual field (P < .001), and inferior visual field (P < .001). The mean deviation of total (P < .001) and pattern (P < .001) deviation analyses was significantly less between fellow eyes than between first and second eyes of different patients.

**Conclusions:** Visual function between fellow eyes showed a fair to moderate correlation that was statistically significant. The pattern of vision loss was also more similar in fellow eyes than between eyes of different patients. These results may help allow better prediction of visual outcome for the second eye in patients with NAION.


**NONARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY (NAION) is the most common acute optic neuropathy in patients older than 50 years. This condition typically presents with sudden painless monocular visual loss accompanied by disc edema and disc-related visual field loss.** A repeat episode of NAION in an already affected eye is distinctly unusual, but occurrence in the fellow eye is common. The frequency of such a contralateral event has been investigated in a number of studies, ranging from 10.5% to 73% of patients. In contrast, to our knowledge, few studies have addressed the degree to which visual loss in a second-affected eye is similar to that in the first.

The large, prospective, randomized trial concerning surgical treatment for NAION (the Ischemic Optic Neuropathy Decompression Trial) generated a large amount of data concerning the frequency and possible risk factors for second-eye NAION but less information regarding a comparison of visual function between the 2 eyes. In this study, a post hoc analysis of visual outcome in patients with bilateral sequential NAION revealed a difference in Snellen acuity of 3 lines or less in approximately half of cases and greater than 6 lines in approximately one-third. Quantitative visual field analysis was not included. In the small number of preceding studies of NAION that included information about visual function in fellow eyes, some noted a correlation among outcomes, whereas others found the opposite. Two studies have specifically addressed the issue of concordance of visual loss between pairs of eyes affected by NAION, including analysis of visual acuity and visual field data, and arrived at conflicting conclusions.

More reliable information regarding the similarity of visual outcomes in fellow eyes with NAION would be useful for counseling patients after a first episode and for evaluating possible treatments for this disorder. To better define the concordance of visual loss in this condition, we reviewed our cases of bilateral sequential NAION, including measures of visual acuity, papillary function, and pattern and severity of visual field loss.

**METHODS**

We retrospectively reviewed the medical records of 102 patients with a diagnosis of bilateral sequential NAION seen at the Midwest Eye Institute, the Neuro-ophthalmology Section, Midwest Eye Institute (Dr Purvin), Indiana University School of Medicine, and Neuro-ophthalmology Section, Midwest Eye Institute (Dr Purvin), Indianapolis; and Department of Neuro-ophthalmology, Hôpital Ophtalmique Jules Gonin, Lausanne, and Department of Clinical Science and Ophthalmology, University of Umea, Umea, Switzerland (Dr Kawasaki).
Institute since 1987. All patients were examined by one of us (V.A.P. or A.K.) during at least 1 attack. The diagnosis of NAION was based on a history of acute unilateral visual loss accompanied by optic disc edema. Compressive lesions, demyelinating disease, and other systemic inflammatory disorders were excluded based on clinical features and appropriate laboratory testing. The study protocol was approved by the institutional review board of Indiana University and is adherent to the tenets of the Declaration of Helsinki.

Sixteen patients were excluded for the following reasons: 5 patients underwent surgical intervention (optic nerve sheath fenestration in 1 and radial optic neurotomy in 4), 7 patients had a concurrent neurovascular source of visual loss, 2 patients had complex or ambiguous clinical features, and 2 patients had unreliable or no Goldmann visual field (1 each). Medical intervention (eg, aspirin, corticosteroids, pentoxifylline, or brimonidine tartrate) was not considered an exclusionary criterion. No patient received intravitreal treatment. Thus, 86 patients were included in the study for analysis. In 62 of the 86 patients, both episodes of NAION were witnessed by one of us (V.A.P. or A.K.); in the remaining 24, optic neuropathy in the fellow eye was discovered during the evaluation for the second event. Other causes of optic neuropathy were excluded in these eyes based on clinical information and ancillary testing, and these patients were assumed to have had a previous, subclinical attack of NAION. Data were collected and statistical analysis performed for each of these subgroups (termed, for the purpose of this study, the witnessed and unwitnessed groups).

The following data were recorded for each patient: age, sex, ethnicity, and laterality of first episode. Outcome measures were visual acuity, visual field, color vision, and relative afferent pupillary defect (RAPD). Visual acuity was measured using best-corrected Snellen acuity, which was also converted to logMAR units for statistical purposes. Counting fingers was assigned a value of 2.0; hand motions, 2.3; and light perception, 2.6. Color vision was measured with Ishihara color plates (Kanehara and Company) and recorded as a fraction of the number of correct answers over the total number of color plates tested. Manual kinetic visual fields (Goldmann perimeter; Haag-Streit International) were measured by a single perimetrist. These visual outcome measures were recorded at the initial and final visits for each patient. The RAPDs were classified into 3 groups: absent or small, 1.5 to 2.4 was designated as medium, and 2.7 or larger was considered large. For those recorded as trace to 4 or greater, none to 1 or greater was considered absent or small, 2 or greater was considered medium, and 3 or greater to 4 or greater was considered large.

Fields were assessed quantitatively using the numerical Goldmann visual field scoring system previously described by Esterman. This method measures the area contained within the 14e isopter using a grid composed of 100 dots. The grid is copied onto a transparency that is overlaid on the Goldmann field, and dots that fall completely within the 14e isopter are counted. A perfect score using this template would be 100.

We calculated the total visual field score and the score per quadrant (superior, inferior, nasal, and temporal) for each eye. On the basis of these scores, we calculated the total deviation and pattern deviation between fellow eyes of the same patient and between the first eye of one patient and an unrelated second eye of a different patient. For the total deviation, the absolute difference between the first and second eyes of the same patient was calculated for each quadrant. Summing the 4 quadrants, an overall total deviation was found for each pair of eyes. The total visual field deviation was calculated for the first eye paired with the second eye (cases: 86 pairs) and with the unrelated second eye of each of the other 85 patients (controls: 86 × 85 = 7310 pairs). For the pattern deviation, the quadrant data (superonasal, superotemporal, inferonasal, and inferotemporal) were first normalized by taking the quadrant with the most points seen and setting that quadrant as the baseline. For the other 3 quadrants, the number of points seen was adjusted to maintain the relative difference to the baseline. Again, the pattern deviation of the visual field was calculated between the first and second eyes of the same patient (cases: 86 pairs) and between the first eye of each patient and the second unrelated eye of all 85 other patients (controls: 86 × 85 = 7310 pairs). This method allowed the pattern differences to be studied while minimizing the difference in overall severity of visual field loss. This technique is analogous to the corrected pattern deviation analysis of the Humphrey visual field analyzer.

The data were analyzed using nonparametric Spearman rank correlation coefficients for all measured parameters of visual function between fellow eyes. The GraphPad InStat computer program (GraphPad Software) was used for statistical analyses. Hemifield concordance was calculated using the Cohen κ test. The pattern of visual field loss was analyzed between fellow eyes of the same patient and between the first eye of one patient and the second unrelated eye of another patient using a technique adapted from the Humphrey visual field analyzer to determine the total deviation and pattern deviation of visual loss for each eye.

## RESULTS

### DEMOGRAPHICS

The mean age of the patients was 62.9 years (range, 35-84 years) (Table 1). Of the 86 patients, 52 (60%) were male and 34 (40%) were female. Eighty-three patients (97%) were white and 3 (3%) were Hispanic. In 47 of 86 patients (55%), the right eye was the first eye to develop NAION; in 39 of 86 patients (45%), the right eye was the second involved eye.

### VISUAL ACUITY

Average Snellen visual acuity was 20/100 for the first eye attack and 20/80 for the second eye attack. With conver-

<table>
<thead>
<tr>
<th>Table 1. Demographics of 86 Patients</th>
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<tr>
<td><strong>Demographic</strong></td>
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<td>------------------</td>
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<tr>
<td>Age, mean (SD) [range], y</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Male</td>
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<td>Female</td>
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<td>Ethnicity</td>
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<td>Hispanic</td>
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<td>First eye to develop NAION</td>
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<tr>
<td>Right</td>
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<td>Left</td>
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<tr>
<td>Time between first and second attacks, mean (SD) [range], mo</td>
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Abbreviation: NAION, nonarteritic anterior ischemic optic neuropathy.

a Data are given as number (percentage) of patients unless otherwise indicated.

b N=71 patients.
Table 2. Summary of Data for All Cases

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>P Value (Wilcoxon Matched Pairs Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LogMAR visual acuity</td>
<td>0.72 (0.77)</td>
<td>.41</td>
</tr>
<tr>
<td>Global visual field</td>
<td>30.1 (21.4)</td>
<td>.12</td>
</tr>
<tr>
<td>Superior visual field</td>
<td>15.1 (10.0)</td>
<td>.50</td>
</tr>
<tr>
<td>Inferior visual field</td>
<td>15.8 (14.3)</td>
<td>.13</td>
</tr>
<tr>
<td>Color plates</td>
<td>0.48 (0.44)</td>
<td>.55</td>
</tr>
</tbody>
</table>

**VISUAL FIELD**

The mean total visual field score (of 100 units) was 30.1 (range, 0–79) for the first eye and 33.8 (range, 0–70) for the second eye. The total visual field score (Figure 1) between the first and second eyes of each patient was significantly correlated (r = 0.50, P < .001, Spearman correlation).

The mean superior visual field score (of a maximum of 33 total units) was 15.1 (range, 0–29) for the first eye and 15.8 (range, 0–29) for the second eye. The superior visual field score (Figure 2) between fellow eyes was significantly correlated between the first and second eyes (r = 0.5450, P < .001, Spearman correlation).

The mean inferior visual field score (of 67 total units) was 15.8 (range, 0–50) for the first eye and 18.0 (range, 0–50) for the second eye. The inferior visual field score between fellow eyes was significantly correlated between the first and second eyes (r = 0.46, P < .001). Hemifield concordance between fellow eyes was low (Cohen κ = 0.25). The mean (SD) total visual field deviation between fellow eyes of the same patient was 19.7 (14.1), whereas the mean (SD) total deviation between the first eye of each patient and the second unrelated eye of all other patients was 25.8 (15.2) (P < .001, t test) for all cases (Figure 3) and 29.5 (16.3) (P < .001, t test) for witnessed cases only. In other words, the total deviation was significantly less between fellow eyes of the same patient compared with the first eye of one patient and the second unrelated eye of another patient. The visual field in the second eye more closely resembled the deviation in the fellow eye of the same patient than the deviation of the first eye of a different patient.

The mean (SD) pattern visual field deviation between fellow eyes was 18.3 (12.3) (P < .001, t test) for all cases (Figure 4) and 16.8 (11.4) for witnessed cases only, whereas the mean (SD) pattern deviation between the first and second eyes of different patients (all pairings) was 25.8 (15.2) (P < .001, t test) and 26.4 (15.6) (P < .001, t test). The adjusted pattern difference was significantly less between fellow eyes of the same patient compared with the first eye of one patient and the second eye of an unrelated patient. In other words, the visual field pattern in the second eye more closely resembled the pattern in the fellow eye than the pattern of the first eye of a different patient.

**RELATIVE AFFERENT PUPIL DEFECT**

The RAPD was absent or small in 69 of 84 patients (82%) for whom quantitative RAPD measurements were available. The RAPD was medium in 15 patients (18%) and large in 0 patients. The RAPD was in the first affected eye in 31 patients and in the second eye in 37 patients.

**COLOR PLATES**

Color plate results (reported as a percentage) demonstrated a low correlation between the first and second eyes (first eye, 48%; second eye, 51%; P = .02, Spearman correlation r = 0.24).
TREATMENT MODALITIES

All treatments were documented, including systemic and ocular modalities. Treatments included systemic corticosteroids in 48 eyes, topical medications (brimonidine, carboxic anhydrase inhibitors, β-blockers, and prostaglandin inhibitors) in 46 eyes, aspirin (4 eyes), acetazolamide (1 eye), pentoxifylline (8 eyes), levodopa-carbidopa (1 eye), and continuous positive airway pressure for sleep apnea (1 eye).

Only 1 eye was treated in 37 cases (3 first eyes and 34 second eyes). With the paired t test, no difference was found between the treated and untreated eyes with respect to global visual field scores (38.3 vs 32.3, \( P = .21 \)). In addition, no difference was seen in logMAR visual acuity (0.68 vs 0.86, \( P = .28 \), Wilcoxon matched pairs test) or in color vision (0.49% vs 43%, \( P = .35 \), Wilcoxon matched pairs test). The results were confounded by the fact that the treated eyes were usually the second involved eye, although the second eyes did not differ from the first eyes overall.

SUBANALYSIS

Outcome measures were compared for those patients in whom both NAION episodes were witnessed vs those with a presumed previous fellow eye event (unwitnessed group). Visual acuity results between the 2 groups had similar Spearman correlation coefficients (\( r = 0.33, P = .008 \) for the witnessed group and \( r = 0.27, P = .20 \) for the unwitnessed group), as were total visual field scores (\( r = 0.62, P < .001 \) for the witnessed group and \( r = 0.23, P = .29 \) for the unwitnessed group). Hemifield concordance (Cohen \( \kappa \)) between the unwitnessed group was 0.05 (none to weak concordance). Mean total visual field deviation between fellow eyes of the same patient and first and second eyes of unrelated patients was also similar in the 2

![Figure 3](image-url3.png)

**Figure 3.** Total deviation between fellow eyes compared with the first and second eyes of different patients. The mean (SD) fellow eye total deviation was 19.7 (14.1). The mean (SD) other eyes total deviation was 30.1 (16.8) \( (P < .001) \).

![Figure 4](image-url4.png)

**Figure 4.** Pattern deviation between fellow eyes compared with the first and second eyes of different patients. The mean (SD) fellow eye pattern deviation was 18.3 (12.3). The mean (SD) other eyes pattern deviation was 25.8 (15.2) \( (P < .001) \).
groups. Color vision results did not correlate significantly between the 2 eyes for either group. Because results for these statistical analyses were the same in witnessed and unwitnessed groups, we combined the 2 groups for interpretation of results.

COMMENT

In our series of 86 cases of bilateral sequential NAION, we found a high degree of concordance between the visual outcomes in fellow eyes. This finding was demonstrated in measures of visual acuity, the magnitude and pattern of visual field loss, and the magnitude of the RAPD. In some respects, this seems to be intuitive, given that optic disc structure and systemic vascular risk factors for NAION would be the same for both eyes. On the other hand, one could imagine a difference in the second affected eye based on either intervention after the first event or progressive age-related attrition of retinal ganglion cells, thus diminishing the optic disc crowding that predisposes patients to this disorder. Were this the case, we would expect the outcome to be better in the second affected eye.

This issue has been previously addressed with conflicting results, potentially supporting either supposition. Boone et al10 reported their findings in 16 patients with bilateral NAION, noting a high degree of congruity between the 2 eyes. Specifically, these authors found that the mean visual field defect in the 2 eyes (assessed with automated perimetry) was within 5 dB in 75% of patients. Similarly, visual acuity was within 3 lines in 81% of cases. In contrast, WuDunn et al11 found less congruity in their analysis of data from 31 patients. In their study, visual acuity was better in the first eye in 32%, better in the second eye in 61%, and the same in 6%. These authors found that the subgroup of patients in whom visual outcome was better in the second eye was significantly older than those with better outcome in the first eye.

At first inspection, it would seem that our findings more closely match those of Boone et al.10 On the other hand, a reanalysis of the findings by WuDunn et al11 suggests that their results are not as disparate as they might appear. Specifically, review of their data concerning visual acuity using the same criterion used by Boone et al indicates that in 16 of 31 patients (52%), visual acuity was within 3 lines in the 2 eyes. In addition, inspection of data concerning visual field results (Figure 2) reveals 2 extreme outliers in whom the mean deviation in the second eye was better by more than 25 dB. Recalculation with these 2 data points excluded reveals a much closer congruity, with the Spearman correlation coefficient improving from \( r = -0.05 \) to 0.43 (\( P = .11 \)).

Despite some similarities, WuDunn et al concluded, based on a review of all their data, that there was in fact a poor correlation in the visual outcomes in the 2 eyes. What might account for our different conclusions? One difference concerns outcome measures. We used quantified Goldmann perimetry, which assesses the entire extent of the visual field and thus may better capture the extent of visual loss compared with the mean defect in automated threshold perimetry, which may underestimate the loss because only the central field is assessed. Another potential difference is the larger number of patients in our study. The study by Boone et al10 included 16 patients and that by WuDunn et al11 included 31, but reliable visual field data were available in only 17 patients in the latter study compared with 86 patients in our study, of whom all had visual field data available for analysis.

On the basis of our data, it does not appear that medical treatment afforded any benefit in terms of visual outcome. Because a number of different treatment modalities were used, but analysis of visual outcome considered the entire group of patients, it is not possible to draw conclusions regarding specific treatments.

In summary, in our comparison of the visual outcome in a large group of patients with bilateral sequential NAION, we found a high degree of concordance between fellow eyes based on measurements of visual acuity, pattern and severity of visual field defect, and RAPD magnitude. This information can be useful for counseling patients after a first episode of NAION, although not much comfort to those at the severe end of the spectrum of visual loss in this condition. More important, these data may be helpful for assessing possible efficacy of novel treatments for NAION. Such treatments would include preventive measures initiated after a first event and interventions that are given for an acute event in the second eye. As novel neuroprotective agents are developed, such data will be particularly useful.

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REFERENCES