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Nonarteritic Anterior Ischemic Optic Neuropathy: *Natural History of Visual Outcome*

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Abstract

Objective—To investigate systematically the natural history of visual outcome in nonarteritic anterior ischemic optic neuropathy (NAION).

Design—Cohort study.

Participants—Three hundred forty consecutive untreated patients (386 eyes) with NAION, first seen in our clinic from 1973 to 2000.

Methods—At first visit, all patients gave a detailed ophthalmic and medical history and underwent a comprehensive ophthalmic evaluation. Visual evaluation was done by recording visual acuity, using the Snellen visual acuity chart, and visual fields with a Goldmann perimeter. The same ophthalmic evaluation was performed at each follow-up visit.

Main Outcome Measures—Natural history of visual acuity and visual field outcome in NAION.

Results—Of the 386 eyes, 332 had 8 weeks or more of follow-up from the initial visit. At the initial visit, in eyes seen ≤ 2 weeks from onset of symptoms, 49% had visual acuity of $\geq 20/30$ and 23% had $\leq 20/200$; in these eyes, 38% had minimal to mild visual field defect and 43% marked to severe defect. In those who were first seen ≤ 2 weeks after onset with visual acuity $\leq 20/70$, there was improvement in 41% at 6 months and in 42% at 1 year after the initial visit. Two years after the initial visit, there was deterioration in 9% of eyes with initial visual acuity of $\geq 20/60$, and in 18% of those with initial visual acuity of $\leq 20/70$. In those who were first seen ≤ 2 weeks of onset with moderate to severe visual field defect, there was improvement in 26% at 6 months and 27% at 1 year after the initial visit. Two years after the initial visit, 27% of eyes with initial minimal to mild field defects showed worsening, as did 19% of those with moderate to severe defects.

Conclusions—About half of the eyes with NAION presented with almost normal visual acuity (20/15 to 20/30) at the initial visit. Thus, the presence of normal visual acuity does not rule out NAION. Visual acuity and visual fields showed improvement or further deterioration mainly up to 6 months, with no significant change after that.

Nonarteritic anterior ischemic optic neuropathy (NAION) is one of the most widespread visually disabling diseases in the middle-aged and elderly population, although no age is immune. Despite a huge volume of literature that has accumulated on its various aspects over the past 3 decades, information on the natural history of visual outcome is scanty, and when available, it is based on retrospective evaluation, usually of a small number of eyes and often from a mixed group of treated (with corticosteroids) and untreated patients.^{1–13} Moreover, the

information about visual improvement or deterioration in these studies is contradictory and confusing. There has been only one recently reported prospective study on the natural history of visual outcome in NAION, which was done as a part of the randomized optic nerve sheath decompression multicenter trial (Ischemic Optic Neuropathy Decompression Trial [IONDT]).^{14,15}

Nonarteritic anterior ischemic optic neuropathy patients are anxious to know their chances of visual improvement or further deterioration. Visual deterioration in NAION may be due to deterioration of visual acuity and/or visual field loss. Therefore, the objective of the present study was to investigate systematically the natural history of both visual acuity and visual field loss in NAION in a large cohort of patients.

Patients and Methods

We have investigated various aspects of NAION systematically in the Ocular Vascular Clinic at the Tertiary Care University of Iowa Hospitals and Clinics since 1973. The current study was part of a prospective study on NAION funded by the National Institutes of Health (RO1 grant), and was approved by the institutional review board. In the present study, we investigated the natural history of visual outcome in NAION; we included patients who were first seen in our clinic from 1973 to 2000. The data on visual outcome were compiled from 340 consecutive NAION patients (294 patients with data for one eye and 46 patients with data from both, a total of 386 eyes) who fulfilled our inclusion criteria for this study.

Criteria required for diagnosis of NAION and inclusion were: (1) A history of sudden visual loss, usually discovered in the morning, and an absence of other ocular, systemic, or neurologic diseases that might influence or explain the patient's visual symptoms; (2) optic disc edema (ODE) at onset must have been documented in the Ocular Vascular Clinic; (3) the eye had optic disc-related visual field defects; (4) there was no neurologic, systemic, or ocular disorder that could be responsible for ODE and visual impairment; and (5) the patient must not have had any corticosteroid therapy or any other treatment for NAION.

We excluded patients who had any retinal or optic nerve lesion or any other factor (e.g., cataract), including any treatment for NAION, that could have influenced the visual status. NAION patients with only background diabetic retinopathy were included, but those who had active neovascularization, vitreous hemorrhages, traction detachment, or other complications influencing the visual acuity or fields were excluded. Patients who had a diagnosis of glaucoma and visual field loss were excluded; however, those with elevated intraocular pressure with a documented normal field before the onset of NAION were included. Eyes with unreliable visual fields were excluded.

Studies Performed

The intention was to document the natural history of visual outcome by recording best-corrected visual acuity and visual field defects on manual kinetic perimetry with a Goldmann perimeter. The data were collected prospectively and systematically. A detailed ophthalmic and medical history was obtained at the patient's first visit to our clinic (by SSH); as part of the medical history, we elicited a detailed history of all previous or current systemic diseases, particularly of arterial hypertension, diabetes mellitus, ischemic heart disease, strokes, transient ischemic attacks, carotid artery disease, and hyperlipidemia. A comprehensive ophthalmic evaluation was performed at that time (by SSH), and included recording of visual acuity using the Snellen visual acuity chart, visual fields with a Goldmann perimeter (using I-2e, I-4e and V-4e targets regularly), relative afferent pupillary defect, and intraocular pressure; slit-lamp examination of the anterior segment, lens, and vitreous; direct and indirect ophthalmoscopy; stereoscopic color fundus photography; and, in acute cases, stereoscopic fluorescein fundus

angiography. When giant cell arteritis was suspected, based on systemic symptoms, elevated erythrocyte sedimentation rate and/or C-reactive protein or suspicion of arteritic AION, a temporal artery biopsy was performed to rule out giant cell arteritis.^{16–18} At each follow-up visit, the same ophthalmic evaluation and stereoscopic color fundus photography were done, except that fluorescein fundus angiography was not performed. At the initial visit, a detailed systemic evaluation was performed by a cardiologist, internist, or the patient's local physician. Where indicated, other systemic or neurologic investigations were done to rule out any systemic or neurologic cause of visual loss.

Follow-up Protocol

Patients were followed initially every 2 to 4 weeks as long as there was ODE, which lasted 7.9 (range, 5.8–11.4) weeks.¹⁹ After that, they were followed at 3 months, 6 months, and then yearly.

Visual Status Evaluation

Visual acuity tested using the Snellen visual acuity chart and under identical testing conditions, almost invariably by the same person (SSH), encouraging the patient to look around and take his or her own time in responding to ensure that the testing provided the most reliable information about the visual acuity. The following steps of visual acuity were checked: 20/15, 20/20, 20/25, 20/30, 20/40, 20/50, 20/60, 20/70, 20/80, 20/100, 20/200, 20/400, counting fingers, hand motion, perception of light, and no perception of light.

Throughout this study, we used kinetic perimetry to measure visual fields. Automated perimetry did not exist when we started the study in 1973; moreover, the changing face of automated perimetry would make such long-term studies difficult. In fact, automated perimetry is still evolving. Both types of perimetry have their advantages and disadvantages, which are discussed elsewhere.²⁰ Visual field plotting was attempted in all patients with a visual acuity of hand motion or better at all visits, with a Goldmann perimeter using I-2e, I-4e, and V-4e targets regularly, although occasionally other targets including I-1e or those in between I-4e and V-4e were used if it was felt that that would provide additional information for evaluation of the visual status. The method of testing visual fields used by us in eyes with NAION is described in detail elsewhere.²¹

Central visual field was also tested by using the Amsler grid chart, which sometimes provided more reliable information than the visual fields.

Visual acuity, visual field defects, and ODE were evaluated separately in a masked fashion; that is, changes in visual acuity, visual fields, and ODE were evaluated independent of each other, so that the severity of one did not influence evaluation of the other. Also, in eyes that developed recurrence of NAION, only the data on visual evaluation collected up to the last follow-up visit of the first episode were used (before the onset of recurrence).

According to our follow-up protocol, these patients were followed initially at 2- to 4-weeks intervals. Therefore, we recorded the date when ODE was last seen and the date when it had completely resolved. For visual assessment when ODE had resolved, visual acuity and visual field were recorded on the visit when ODE had just resolved completely; this date would be within 2 to 4 weeks of the actual resolution of ODE.

A change of ≥ 3 lines in the Snellen visual acuity chart was considered a significant change, which is equivalent to a logarithm of the minimum angle of resolution (logMAR) change of at least 0.30. We divided visual acuity into 2 categories for evaluation purposes: (1) normal visual acuity, defined as $\geq 20/30$, because that category cannot show an improvement of 3 lines to achieve 20/20; or (2) poor visual acuity, defined as $\leq 20/70$ because we wanted to compare our

data with the IONDT study^{14,15} (considered the gold standard by most neuro-ophthalmologists), which used 20/64 as their inclusion criterion.

We wanted to evaluate quantitative and qualitative changes in visual fields plotted with the Goldmann perimeter during the follow-up period. We tried 3 different strategies to determine reliably the extent of visual loss, the amount of visual functional disability caused by the visual field loss, and the change during follow-up. The strategies were: (1) ranking the visual fields in their order from best to worst; (2) the “counting dots” method used for visual field scoring originally described by Esterman²²; and (3) an overall subjective grading of the visual fields. We found that the last method gave the best information, so we used it in this study. This method has proved reliable in our previous studies.^{23–26}

All visual fields plotted during the entire follow-up period were laid out in chronological order, and 3 clinicians experienced in the interpretation of visual fields done with a Goldmann perimeter (Drs. Sohan Hayreh, Stanley Thompson, and Michael Wall) simultaneously scrutinized them, and independently, subjectively graded the severity of visual loss, taking into consideration all the parameters one considers while clinically evaluating a change in visual fields plotted with manual kinetic perimetry (because of the complexity of the Goldmann visual field defects, it is unfortunately difficult to define the exact parameters). Two types of evaluation of visual fields were performed using this method: (1) the entire visual field and (2) central and peripheral fields evaluated separately, to determine whether each one improved, deteriorated, or remained stable. In general, deterioration was defined as development of a new scotoma, a deepening or expanding scotoma, a generalized constriction not accounted for by any other ocular parameter, or overall deterioration. Improvement was the reverse of these changes. Subtle changes were confirmed on more than one examination.

The entire visual field was graded into 5 levels, from 0 (normal) to 4 (severe loss) in steps of 0.5 (and occasionally 0.25 when the differences were subtle), and the dates when each change was noted during the entire follow-up. The grade was judged by qualitatively assessing clinical computation of the amount of visual field loss, factoring in the functional disability produced by that defect; for example, inferior and/or central visual field defect, producing far more functional disability, was assigned a much higher grade than a corresponding loss in the upper field or elsewhere. The grading was started from the first visual field. A change from one grade to another was noted. Then the 3 graders compared their grades immediately. If there was a disagreement, it was resolved by discussion at that time to reach a unanimous agreement. The findings were then condensed for descriptive purposes into minimal (grade 0.5), mild (grades >0.5–1.0), moderate (1.5–2.0), marked (2.5–3.0), and severe (3.5–4.0) loss. These grades are best described by examples given elsewhere.²³

Statistical Methods

Descriptive statistics (means, standard deviations, and percentages) were computed for the demographic and clinical variables, visual acuity, and visual field defect at initial visit. Changes in visual acuity and visual field defect were assessed from initial visit to ODE resolution, from ODE resolution to 3 months, 9 months, and 2 years after resolution of ODE, and also for the overall follow-up at 3, 6, 12, and 24 months from initial visit. Because patient visits did not exactly fall at the specified time period for various logistic, seasonal, or geographic reasons, a ± 6 -week interval was used for the 3-, 6-, and 9-month follow-up visits and ± 12 weeks for the 1- and 2-year follow-up visits. A change of ≥ 3 lines in the Snellen visual acuity chart was considered a significant change in either direction (improved or deteriorated), which is equivalent to a logMAR change of ≥ 0.30 . At these same intervals, change in visual field loss was also examined, and a difference in grade of ≥ 0.5 , in either direction, was defined as improvement or deterioration. The percentages of improved and worse visual outcomes were calculated at each of these intervals. Only the eyes that had at least that length of follow-up for

the specified interval were included in the computation. The changes were not carried over if the patient did not have follow-up for the later time period. These are reported separately for those first seen within 2 weeks of onset of visual loss and those first seen >2 weeks after visual loss. To test for the association of gender, age, smoking, and systemic diseases with visual outcome, 2-way analysis of variance was used for age, and the Cochran-Mantel-Haenszel test was used for the other variables, adjusting for initial visual acuity/visual field grade.

Results

Demographic characteristics of the study patients are summarized in Table 1. Of the 386 eyes, 332 had 8 weeks or more of follow-up from the initial visit, with 290 eyes having ≥ 6 weeks of follow-up after ODE had resolved. During follow-up, NAION recurred in 6% (25 of 386 eyes); for these 25 eyes only, the data collected up to the last follow-up visit before recurrence were used in the statistical analysis.

At the initial visit, eyes that were seen within 2 weeks after onset of symptoms had visual acuity of $\geq 20/20$ in 32%, and 20/25 to 20/30 in 17% (Table 2). Visual acuity of $\leq 20/200$ was present in 23% of eyes. Visual field defect was minimal to mild in 38% and marked to severe in 43%.

Assessment of Change in Visual Acuity

This was divided into 3 phases: (1) from initial visit to ODE resolution (Table 3 [available at <http://aaojournal.org>]); (2) from the time when ODE resolved to 3 months, 9 months, and 2 years after resolution (Table 4 [available at <http://aaojournal.org>]); and (3) overall change at 3 months, 6 months, 1 year, and 2 years from the initial visit (Table 5).

From Initial Visit to Resolution of Optic Disc Edema—Detailed findings are given in Table 3. Of the eyes that presented within 2 weeks of onset of symptoms and initial visual acuity of $\leq 20/70$, 21% showed improvement from first visit to the time when ODE resolved, whereas 4% got worse; however, when the initial visual acuity was $\geq 20/60$, 9% (12 of 130 eyes) got worse. Patients who were first seen >2 weeks (3 weeks to about 10 weeks) after onset of visual loss, might well have experienced improvement and/or deterioration in visual status before they first visited in our clinic. That would have an effect on the percentage of deterioration or improvement that was observed for this group compared to those patients who were first seen within 2 weeks after onset.

From the Time When Optic Disc Edema Resolved to 3 and 9 Months and 2 Years after Resolution—Detailed findings about the visual acuity improvement/deterioration at these time periods are given in Table 4.

Overall Change at 3 and 6 Months and 1 and 2 Years after the Initial Visit—Detailed findings are given in Table 5. In those seen within 2 weeks of onset with visual acuity $\leq 20/70$, there was an improvement in visual acuity in 17% at 3 months, 41% at 6 months, 42% at 1 year, and 36% at 2 years after the initial visit. Two years after the initial visit, worsening of visual acuity was seen in 9% (8 of 89) of those with initial visual acuity of $\geq 20/60$ and in 18% of those with initial visual acuity of $\leq 20/70$.

Assessment of Change in Visual Fields

Like visual acuity, this assessment was also divided into 3 phases. Changes in visual field defect are shown in Tables 6 to 8.

From Initial Visit to Optic Disc Edema Resolution—Detailed findings are given in Table 6 (available at <http://aaojournal.org>). Of the eyes that presented within 2 weeks of onset

of symptoms and had moderate to severe initial visual field loss, 19% showed improvement from first visit to the time when ODE resolved, whereas 14% worsened; however, when the initial visual field loss was minimal to mild 23% (16 of 71) worsened. As discussed, in patients who were first seen >2 weeks (3 weeks to about 10 weeks) after onset of visual loss, lower percentages of both deterioration or improvement were observed for this group than in those first seen within 2 weeks of onset.

From the Time When Optic Disc Edema Resolved to 3 and 9 Months and 2 Years after Resolution—Detailed findings about the visual fields improvement/deterioration at these time periods are given in Table 7 (available at <http://aojournal.org>).

Overall Change at 3 and 6 Months and 1 and 2 Years from the Initial Visit—

Detailed findings are given in Table 8. Of those who were first seen within 2 weeks of onset with moderate to severe visual field defect, there was improvement in 21% at 3 months, 26% at 6 months, 27% at 1 year, and 22% at 2 years from initial visit. In eyes with minimal to mild field defects initially, there was worsening in 26% (17/65) at 3 months and similarly at 2 years (27%; 12/45) after the first visit.

We also evaluated overall changes in central 30° and the peripheral visual fields separately during follow-up. The central field was stable during the follow-up period in 68% of the eyes, improved in 16%, and worsened in 16%. There was improvement in peripheral field in 17% of the eyes and worsening in 18%.

In the present study, we found that of the eyes with visual acuity improvement, the apparent improvement was due to eccentric fixation in 26%; that is, there was no improvement in the region of central fixation. In those with visual acuity of $\leq 20/70$, excluding those with visual improvement owing to eccentric fixation, the genuine improvement was in 30% of eyes.

The association of demographic and systemic conditions with visual outcome at 1 year after the initial visit was examined in those seen within 2 weeks of onset of NAION with initial visual acuity of $\leq 20/40$. After adjusting for the effect of initial visual acuity, visual acuity change at 1 year did not show a significant association with gender ($P = 0.44$), age at diagnosis ($P = 0.35$), smoking ($p = 0.53$), diabetes mellitus ($P = 0.35$), arterial hypertension ($P = 0.38$), ischemic heart disease ($P = 0.91$), hyperlipidemia ($P = 0.61$), or migraine ($P = 0.21$). For visual field change at 1 year, except for migraine, where the statistical test suggested a possible association (worsening in 4/7 [57%] with migraine vs 27/135 [20%] without; $P = 0.09$), no significant association was observed in the other variables (all $P > 0.42$).

Discussion

The most important piece of information required in NAION, from the point of view of both patient and ophthalmologist, is the natural history of visual outcome. This information is also vital to determine if any treatment modality advocated for NAION is beneficial.^{14,15} In the vast majority of published reports, visual outcome in NAION has essentially been described in terms of only visual acuity. Moreover, the vast majority of studies are based on retrospective evaluation, usually of a small number of eyes, some treated (with corticosteroids) and some not.^{1–13} By contrast, in our study, all patients were evaluated by recording visual fields as well as best-corrected visual acuity, initially and at each follow-up visit. It is established that visual acuity gives information basically about the functioning of only the fovea and the papillomacular nerve fibers in the optic nerve, and not of the entire retina or the entire optic nerve. Nonarteritic anterior ischemic optic neuropathy may involve the entire optic nerve head or only one part of it; in some cases, the papillomacular nerve fibers may not be involved at all, which explains the presence of normal visual acuity in many eyes with NAION (Table 2)

(Tables 3, 4 [available at <http://aaojournal.org>]). Information about the function of the entire optic nerve is provided only by the visual fields. So visual acuity and visual fields provide very different information about the visual status of an eye, and the two can be totally independent of each other. For example, an eye can have massive visual field loss (e.g., absolute altitudinal defect or even more) but sparing central fixation, resulting in normal visual acuity despite complete loss of half or more of the visual field in the eye. We have seen eyes with NAION where only the central 5° to 10° visual field is left, but the visual acuity was 20/15 to 20/20. Visual fields plotted with manual kinetic perimetry provide information of both central as well as the entire visual field function, whereas automated perimetry misses all the information beyond 24° to 30° in the periphery. In NAION, it is essential to assess not only the central field, but the peripheral field as well. Therefore, to assess visual disability caused by NAION, one needs information on both visual acuity and the entire peripheral visual field. We have discussed at length the clinical significance of central versus peripheral visual field loss in NAION.²¹ It is well established that constant tracking provided by the peripheral visual fields is essential for sensory input to our day-to-day activity and navigation, which makes peripheral visual fields vital for routine activities except for what requires fine visual acuity.

Changes in Visual Acuity and Visual Fields during Follow-Up

Table 2 gives information about the visual acuity and visual field status at the initial visit to our clinic. This shows that almost half of the NAION eyes initially presented with a visual acuity of 20/15 to 20/30, a fact not fully appreciated in the ophthalmic community and sometimes responsible for missing the diagnosis of NAION, because of the prevalent belief that every eye with ischemia of the optic nerve head (as in NAION) cannot have normal visual acuity. By contrast, all eyes with classic NAION do have a visual field loss of variable severity; however, eyes with incipient NAION initially present with normal visual acuity and visual field.²⁷ Available evidence indicates that incipient NAION is the earliest, asymptomatic clinical stage in the evolution of the NAION disease process, but the vast majority of patients are never seen during that stage because they have no visual symptoms.²⁷ In the present study, the “date of onset” used for evaluation of visual improvement or deterioration is the date when the eye developed visual loss. A detailed account of the pattern and prevalence of visual field abnormalities at the initial visit in our study is given elsewhere.²¹ Briefly, NAION eyes can present with a variety of optic nerve head related visual field defects. We found that a combination of relative inferior altitudinal defect with an absolute inferior nasal defect is usually the most common pattern.

Tables 3 through 8 give detailed information about the changes during follow-up, in the visual acuity and visual fields, analyzed according to different variables. Although eyes with normal or mild deterioration of visual function are not going to show improvement, eyes with moderate to severe visual loss can show improvement, and more likely vice versa for deterioration. Eyes with a visual acuity of $\leq 20/70$ showed improvement in 41% for up to 6 months after the initial visit and stabilized thereafter (Table 5). In eyes with moderate to severe visual field defect, there was improvement in 26% up to 6 months after initial visit and stabilization thereafter (Table 8). Thus, overall eyes with NAION can show visual function improvement up to about 6 months from the initial visit, but not thereafter.

This data analysis is based on the overall visual field loss. In addition, we analyzed the data according to the subjective clinical evaluation of changes in the central and peripheral visual fields, separately, during the follow-up period. This showed that, during the follow-up period, the central visual field remained stable in 68%, improved in 16%, and worsened in 16%. There was improvement in peripheral visual field in 17% of the eyes and worsening in 18%.

As mentioned, visual acuity and visual fields provide very different information about the visual status in NAION. Therefore, the changes in the two can be totally independent and

unrelated. Also, the amount of visual acuity and visual field change seen during follow-up in a patient depends on the time when a patient is first seen after the onset of visual loss. In our study, patients who were first seen >2 weeks (3 weeks to about 10 weeks) after the onset of visual loss and still had ODE showed both less improvement and less deterioration in visual acuity and visual fields than those first seen within 2 weeks of onset (Tables 3,6 [available at <http://aaojournal.org>]). Obviously, the longer the time interval between onset and first evaluation, the greater the likelihood of visual changes having occurred already, and, hence, the smaller the chance of change in visual status from then on. We found that the visual change does not always mean either improvement or deterioration throughout the entire course of initial follow-up, but may show a changing pattern; for example, in some eyes there was improvement or deterioration at one time and vice versa at another time in the same eye. The findings in our study represent the initial and final visual status only.

In our experience of dealing with eyes with both NAION and arteritic AION, we have found the following two phenomena, from time to time.

1. The recorded improvement in visual acuity does not always reflect genuine improvement in optic nerve function. It may simply be due to the patient having learned by experience to read the test chart better by looking around and fixating eccentrically. This applies particularly to an eye with a visual field defect passing through or just involving the central fixation spot, as for example in altitudinal visual field defects or a small central scotoma. In such cases, by eccentric fixation, the patient may finally test much better without any actual improvement in the retinal or optic nerve function. In our studies on various types of ocular vascular disorders, we have found that, for genuine visual acuity improvement, there must be simultaneous improvement in both the central scotoma and visual acuity.^{28,29} In our study, improvement was due to eccentric fixation in 26% of the eyes with visual acuity improvement. This is further supported by the following two findings. First, visual acuity of $\leq 20/70$ improved in 42% (Table 5), but if one excludes those with visual improvement owing to eccentric fixation, the genuine improvement is in about 30%. This corresponds closely to the percentage with improved visual fields (27%; Table 8) during follow-up. Second, the incidence of worsening of visual acuity and visual field is the same because that reflects the actual state of the patient's visual status (Tables 5-8). That is why we strongly emphasize that improved visual acuity without corresponding improvement of central visual field defects on perimetry or on Amsler chart can be misleading.^{28,29}
2. In our study, we also found that in some patients with bilateral NAION, when the second eye developed NAION with marked deterioration of visual acuity, the previously involved eye with comparatively better visual acuity showed spontaneous improvement. In NAION and other ocular vascular disorders studied in our Ocular Vascular Clinic since 1973, we have found that sometimes the first eye with poor visual acuity may develop a variable degree of amblyopia, even in the middle-aged and elderly population, because the patient may not use that eye for central vision when the fellow eye has normal visual acuity (a phenomenon similar to occlusion amblyopia in children); however, when the fellow eye develops marked visual loss from NAION, the amblyopic eye with comparatively better visual acuity soon shows a variable amount of spontaneous improvement. This has erroneously been attributed to some treatments.³⁰

There is only one other large prospective natural history study on outcome of visual acuity in NAION,^{14,15} done as a part of the randomized IONDT. The outcome of a study depends on its design. The primary objective of the IONDT study was to "assess the safety and efficacy of optic nerve decompression surgery compared with careful follow-up alone in patients with"

NAION. By contrast, primary objective of our study was to determine the natural history of visual outcome in NAION as a whole. The study design, inclusion and exclusion criteria, and several other parameters differ between the two studies. For example, in the IONDT study, to be eligible for inclusion in the study, the visual acuity must have been $\leq 20/64$, age ≥ 50 years, and duration of symptoms < 14 days; therefore, it contained a very selective group of NAION patients. In our study, by contrast, there were no such inclusion/exclusion criteria, because we wanted to determine the natural history of visual outcome in all patients with NAION, irrespective of visual acuity, age, or duration of visual loss. Thus, there are fundamental differences in the designs of the two studies that explain the differences in the results. However, we did compare the visual acuity outcome in the IONDT study with our study, by using only those eyes that had initial visual acuity of $\leq 20/70$ and those seen within 2 weeks of the onset of visual loss, as was the case in the IONDT study. Table 9 shows the comparison of the visual acuity findings of both studies at follow-up at 3, 6, 12, and 24 months after the onset of NAION. Most interestingly, this comparison showed that, despite the age difference between the two studies, the visual acuity outcome was identical in the two studies at follow-up of 6 and 12 months.

In our study, we did not find sufficient evidence to indicate an effect of presence of systemic diseases on the visual outcome in NAION.

Strengths and Limitations

Almost all patients in this study were initially seen and evaluated systematically and serially followed up throughout the duration of the study by the same investigator (SSH). Thus, there was consistency in the quality of evaluation throughout the entire duration of the study, unlike most other studies. Even in IONDT,^{14,15} the fact that it was a multicenter study, meant that it involved multiple persons in collection of visual acuity data at the various study centers.

The limitation in our evaluation of natural history of visual outcome in NAION is that it could not document the visual function from its day of onset of NAION onward. Our visual evaluation can only be from the time the patients were first seen in our clinic and not from the date of onset of visual loss in NAION, so that if there was deterioration or improvement before we saw the patient, that information is not available; there were patients who gave a history of visual deterioration or improvement between onset and when we saw them. Thus, it is possible that our data, particularly in eyes seen >2 weeks after the onset of visual loss, may underestimate the visual change to some extent, both deterioration and improvement, during the very early stages. This may explain the differing findings in visual acuity (Table 3 [available at <http://aaojournal.org>]) and visual fields (Table 6 [available at <http://aaojournal.org>]) in patients seen within 2 weeks from the onset of visual loss versus those seen >2 weeks after the onset.

In conclusion, in classic NAION, about half of the eyes at the initial visit presented with almost normal visual acuity (20/15 to 20/30), but they all had one or another type of optic disc-related visual field defect. Thus, the presence of normal visual acuity does not rule out NAION. In the eyes seen within 2 weeks of onset of visual loss, during a follow-up of 6 months, when visual acuity was $\leq 20/70$, it improved in 41%, deteriorated in 19%, and remained stable in 40%. In eyes with moderate to marked visual field loss, the corresponding figures were 26%, 15%, and 59%, respectively. Visual acuity and visual fields mainly improved or further deteriorated for up to 6 months, with no significant change after that.

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Table 1**Demographic and Clinical Characteristics of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) Patients**

Demographic/Clinical Variable	For 340 Patients (386 eyes)
Gender (male)	198 (58%)
Age at initial visit (mean $\pm$ SD)	61 $\pm$ 12
NAION eye involvement	
Right eye	113 (33%)
Left eye	99 (29%)
Both eyes *	128 (38%)
Follow-up (of eyes with follow-up)	(n = 332 [†] eyes)
Median (25th–75th percentiles)	3.4 (1.3–7.5) yrs
Minimum–maximum	2.3 mos–25 yrs
Systemic conditions	
Arterial hypertension	147 (43%)
Ischemic heart disease	72 (21%)
Diabetes mellitus	115 (34%)
TIA/CVA	30 (9%)
Peripheral vascular disease	17 (5%)
Cholesterol (>200 mg; n = 216 [‡])	152 (70%)
Smoked current/past	166 (49%)
Diabetic retinopathy	44 (11%) eyes
Initial IOP (mean $\pm$ SD)	380 eyes (16 $\pm$ 4)

CVA = cerebrovascular disorder; IOP = intraocular pressure; SD = standard deviation; TIA = transient ischemic attack.

* Of those with bilateral NAION, only one eye was included in the study for 82 of 128 (41 right eyes and 41 left eyes).

[†] There was no follow-up data, or data were <8 wks old, for 54 eyes; these eyes are included only in the analysis of baseline features.

[‡] Owing to various logistic reasons, fasting cholesterol levels information was available in 216 patients.

Table 2**Visual Acuity and Visual Field at Initial Visit**

	Time from Onset of Visual Loss to Initial Visit			
	<i>Within 2 Weeks (n = 237 Eyes)</i>	<i>3–4 Weeks (n = 69 Eyes)</i>	<i>5–8 Weeks (n = 52 Eyes)</i>	<i>≥9 Weeks (n = 28 Eyes)</i>
Visual acuity				
20/15–20/20	76 (32%)	12 (17%)	19 (37%)	7 (25%)
20/25–20/30	40 (17%)	18 (26%)	4 (8%)	3 (11%)
20/40–20/60	42 (18%)	11 (16%)	10 (19%)	5 (18%)
20/70–20/100	20 (8%)	10 (15%)	8 (16%)	3 (11%)
20/200–20/400	25 (9%)	11 (16%)	1 (2%)	7 (25%)
Counting fingers or worse	34 (14%)	7 (10%)	10 (19%)	3 (11%)
Visual field defect	(n = 232 eyes) *	(n = 69 eyes)	(n = 51 eyes) *	(n = 27 eyes) *
Minimal	18 (8%)	2 (3%)	2 (4%)	1 (4%)
Mild	70 (30%)	19 (28%)	20 (39%)	5 (19%)
Moderate	44 (19%)	9 (13%)	10 (19%)	5 (19%)
Marked	67 (29%)	33 (48%)	14 (27%)	10 (37%)
Severe	33 (14%)	6 (8%)	5 (10%)	6 (22%)

* Missing visual field defect data in 7 eyes (5, within 2 wks; 1, 5–8 wks; 1, ≥9 wks).

Table 3

Visual Acuity Change from Initial Visit to Optic Disc Edema Resolution

Visual Acuity at Initial Visit	n	Seen ≤2 Weeks from Onset (n = 201 Eyes)		Seen >2 Weeks from Onset (n = 131 Eyes)	
		No. (%) of Eyes		No. (%) of Eyes	
		Improved	Worsened	Improved	Worsened
20/15–20/30	96	—	9 (9%)	56	3 (5%)
20/40	23	2 (9%)	2 (9%)	8	1 (12%)
20/50–20/60	11	1 (9%)	1 (9%)	15	1 (7%)
20/70–20/100	17	2 (12%)	1 (6%)	18	0 (0%)
20/200–400	22	5 (23%)	2 (9%)	17	0 (0%)
Counting fingers or worse	32	8 (25%)	0 (0%)	17	0 (0%)
≤20/50	82	16 (20%)	4 (5%)	52	1 (1%)
≤20/70	71	15 (21%)	3 (4%)	52	0 (0%)

Table 4

Visual Acuity (VA) Change from VA at Optic Disc Edema (ODE) Resolution to 3 and 9 Months, and 2 Years after ODE Resolution

Visual Acuity at ODE Resolution	3 Months* after ODE Resolution (n = 290 [†] Eyes)			9 Months* after ODE Resolution (n = 255 [†] Eyes)			2 Years* after ODE Resolution (n = 197 [†] Eyes)		
	No. (%) of Eyes			No. (%) of Eyes [†]			No. (%) of Eyes		
	n [†]	Improved	Worsened	n [†]	Improved	Worsened	n [†]	Improved	Worsened
20/15-20/30	138	—	0 (0%)	121	—	1 (1%)	102	—	1 (1%)
20/40	30	2 (7%)	1 (3%)	25	3 (12%)	1 (4%)	17	2 (12%)	1 (6%)
20/50-20/60	20	1 (5%)	0 (0%)	18	1 (6%)	0 (0%)	14	1 (7%)	0 (0%)
20/70-20/100	30	2 (7%)	1 (3%)	27	3 (11%)	2 (7%)	20	3 (15%)	2 (10%)
20/200-20/400	33	6 (18%)	4 (12%)	29	7 (24%)	7 (24%)	19	5 (26%)	7 (37%)
Counting fingers or worse	39	7 (18%)	1 (3%)	35	12 (34%)	4 (11%)	25	9 (36%)	3 (12%)
≤20/50	122	16 (13%)	6 (5%)	109	23 (21%)	13 (12%)	78	18 (23%)	12 (15%)
≤20/70	102	15 (15%)	6 (6%)	91	22 (24%)	13 (14%)	64	17 (27%)	12 (19%)

* ±6 wks for 3 and 9 mos; ±12 wks for 2 yrs.

[†] Includes the eyes with a post-ODE resolution follow-up for VA of at least the lower limit specified.

Table 5

Visual Acuity (VA) Change from VA at Initial Visit to 3 and 6 Months and 1 and 2 Years after First Visit

Time from First Visit/Initial VA	n*	Seen ≤2 Weeks from Onset		Seen >2 Weeks from Onset	
		No. (%) of Eyes		No. (%) of Eyes	
		Improved	Worsened	Improved	Worsened
3 mos [†]	(n = 194)				
20/15–20/30	95	—	8 (8%)	—	2 (4%)
20/40	23	3 (13%)	2 (9%)	0 (0%)	1 (12%)
20/50–20/60	11	0 (0%)	1 (9%)	2 (15%)	1 (8%)
20/70–20/100	16	1 (6%)	1 (6%)	5 (29%)	0 (0%)
20/200–20/400	21	5 (24%)	1 (5%)	1 (7%)	0 (0%)
CF or worse	28	5 (18%)	0 (0%)	2 (13%)	0 (0%)
≤20/50	76	11 (14%)	3 (4%)	10 (17%)	1 (2%)
≤20/70	65	11 (17%)	2 (3%)	8 (17%)	0 (0%)
6 mos [†]	(n = 177)				
20/15–20/30	88	—	7 (8%)	—	2 (4%)
20/40	21	3 (14%)	2 (10%)	0 (0%)	1 (17%)
20/50–20/60	9	2 (22%)	0 (0%)	3 (30%)	1 (10%)
20/70–20/100	15	4 (27%)	2 (13%)	2 (17%)	0 (0%)
20/200–20/400	17	6 (35%)	5 (29%)	5 (42%)	1 (8%)
CF or worse	27	15 (56%)	2 (7%)	3 (20%)	2 (13%)
≤20/50	68	27 (40%)	9 (13%)	13 (27%)	4 (8%)
≤20/70	59	25 (41%)	9 (19%)	10 (26%)	3 (8%)
1 yr [†]	(n = 166)				
20/15–20/30	82	—	6 (7%)	—	2 (4%)
20/40	21	5 (24%)	3 (14%)	0 (0%)	1 (17%)
20/50–20/60	8	2 (25%)	0 (0%)	2 (20%)	1 (10%)
20/70–20/100	15	3 (20%)	2 (13%)	1 (9%)	0 (0%)
20/200–20/400	15	6 (40%)	5 (33%)	6 (55%)	2 (18%)
CF or worse	25	14 (56%)	2 (8%)	4 (33%)	0 (0%)
≤20/50	63	25 (40%)	9 (14%)	13 (30%)	3 (7%)
≤20/70	55	23 (42%)	9 (16%)	11 (32%)	2 (6%)
2 yrs [†]	(n = 133)				
20/15–20/30	69	—	5 (7%)	—	1 (3%)
20/40	16	4 (25%)	3 (19%)	0 (0%)	0 (0%)
20/50–20/60	4	2 (50%)	0 (0%)	1 (14%)	1 (14%)
20/70–20/100	15	4 (27%)	2 (13%)	2 (22%)	0 (0%)
20/200–20/400	10	3 (30%)	4 (40%)	2 (33%)	2 (33%)
CF or worse	19	9 (47%)	2 (11%)	3 (38%)	0 (0%)
≤20/50	48	18 (38%)	8 (17%)	8 (27%)	3 (10%)
≤20/70	44	16 (36%)	8 (18%)	7 (30%)	2 (9%)

CF = counting fingers.

* Includes the eyes that have a follow-up for VA of at least the lower limit specified.

[†] ±6 wks for 3 and 6 mos; ±12 wks for 1 and 2 yrs.

Table 6

Visual Field Change from Initial Visit to Optic Disc Edema Resolution

Visual Field Defect at Initial Visit	Seen ≤2 Weeks from Onset (n = 200 * Eyes)			Seen >2 Weeks from Onset (n = 129 * Eyes)		
	No. (%) of Eyes			No. (%) of Eyes		
	n	Improved	Worsened	n	Improved	Worsened
Minimal	15	—	0 (0%)	4	—	1 (25%)
Mild	56	6 (11%)	16 (29%)	39	7 (18%)	4 (10%)
Moderate	39	5 (13%)	8 (21%)	23	2 (9%)	1 (4%)
Marked	60	13 (22%)	10 (17%)	47	10 (21%)	6 (13%)
Severe	30	7 (23%)	0 (0%)	16	2 (13%)	0 (0%)
Moderate to severe	129	25 (19%)	18 (14%)	86	14 (16%)	7 (8%)

* Missing data for visual field defect in 3 eyes (1 seen ≤2 wks from onset; 2 seen >2 wks from onset) for ODE resolution follow-up.

Table 7

Visual Field Change from Visual Field at Optic Disc Edema (ODE) Resolution to 3 and 9 Months and 2 Years after ODE Resolution

Visual Field Defect at ODE Resolution	3 Months* after ODE Resolution (n = 267 [†] Eyes)		9 Months* after ODE Resolution (n = 238 [†] Eyes)		2 Years* after ODE Resolution (n = 188 [†] Eyes)	
	No. (%) of Eyes		No. (%) of Eyes		No. (%) of Eyes	
	<i>n</i> [‡] Improved	Worsened	<i>n</i> [‡] Improved	Worsened	<i>n</i> [‡] Improved	Worsened
Minimal	24—	0 (0%)	22	—	18—	1 (5%)
Mild	704 (6%)	1 (1%)	60	6 (10%)	475 (11%)	4 (8%)
Moderate	530 (0%)	1 (2%)	50	0 (0%)	411 (2%)	4 (9%)
Marked	864 (5%)	2 (2%)	76	6 (8%)	615 (8%)	4 (6%)
Severe	344 (12%)	0 (0%)	30	5 (17%)	213 (14%)	0 (0%)
Moderate to severe	1738 (5%)	3 (2%)	156	11 (7%)	1239 (7%)	6 (5%)

* ±6 wks for 3 and 9 mos; ±12 wks for 2 yrs.

[‡] Includes the eyes that have a post-ODE resolution follow-up for visual field of at least the lower limit specified.

Table 8

Visual Field Change from Initial Visit to 3 and 6 Months and 1 and 2 Years from Initial Clinic Visit

Time from Initial Visit/Initial Visual Field	Seen Within 2 Weeks from Onset			Seen >2 Weeks from Onset		
	* n	No. (%) of Eyes		* n	No. (%) of Eyes	
		Improved	Worsened		Improved	Worsened
3 mos [†]	(n = 180)			(n = 109)		
Minimal	12	—	0 (0%)	4	—	—0 (0%)
Mild	53	7 (13%)	17 (32%)	31	7 (23%)	2 (6%)
Moderate to severe	115	24 (21%)	18 (16%)	74	15 (20%)	8 (11%)
6 mos [†]	(n = 166)			(n = 94)		
Minimal	12	—	0 (0%)	4	—	—0 (0%)
Mild	49	7 (14%)	15 (31%)	27	6 (22%)	2 (7%)
Moderate to severe	105	27 (26%)	16 (15%)	63	13 (21%)	6 (10%)
1 yr [†]	(n = 153)			(n = 87)		
Minimal	11	—	0 (0%)	4	—	—1 (25%)
Mild	46	7 (15%)	15 (33%)	26	6 (23%)	3 (12%)
Moderate to severe	96	26 (27%)	16 (17%)	57	12 (21%)	5 (9%)
2 yrs [†]	(n = 123)			(n = 66)		
Minimal	9	—	0 (0%)	3	—	—0 (0%)
Mild	36	7 (19%)	12 (33%)	20	6 (30%)	2 (10%)
Moderate to severe	78	17 (22%)	15 (19%)	43	9 (21%)	3 (7%)

* Includes the eyes that have a follow-up for visual field of at least the lower limit specified.

[†] ±6 wks for 3 and 6 mos; ±12 wks for 1 and 2 yrs.

Table 9

Comparison of Visual Acuity Change in Nonarteritic Anterior Ischemic Optic Neuropathy* between the Ischemic Optic Neuropathy Decompression Trial (IONDT) and this Study of Natural History

Time from Initial Clinic Visit (mos)	No. of Eyes		Improved		Worsened	
	IONDT	This Study*	IONDT (%)	This Study (%)	IONDT (%)	This Study (%)
3	121	65	40	17	9	3
6	122	59	43	41	15	19
12	114	55	41	42	16	16
24	87	44	31	37	22	18

* In eyes that were first seen within 2 wks of onset of nonarteritic anterior ischemic optic neuropathy with initial visual acuity $\leq 20/70$.