

Anterior Ischemic Optic Neuropathy in Patients Younger than 50 Years

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- **PURPOSE:** To characterize anterior ischemic optic neuropathy (AION) in patients younger than 50 years.
- **DESIGN:** Retrospective study.
- **METHODS:** Records of all AION patients seen between 1989 and 2006 were reviewed. Patients younger than 50 years when initial visual loss occurred were included.
- **RESULTS:** Of 727 consecutive patients with AION, 169 (23%) were younger than 50 years (median, 43 years; range, 13 to 49 years; 58% men; 93% White). Involvement was unilateral in 59% of patients and bilateral in 41%. At least one cardiovascular risk factor was found in 74% of patients. Hypercoagulable states and vasculitis were found in 8%. An underlying small or anomalous optic disk was found in 92% of eyes (210/230). Isolated disk anomalies (without systemic risk factors) were present in 26% of eyes. Final visual acuities were 20/40 or better in 64% of eyes and 20/200 or worse in 22%. Among patients with bilateral involvement, final visual acuity was similar in the two eyes in 70% of patients. Anemia and type I diabetes were associated significantly with fellow eye involvement. Recurrent AION in the same eye occurred in 6% of patients.
- **CONCLUSIONS:** AION in younger patients is not uncommon and represents 23% of AION patients in a tertiary neuro-ophthalmic service. Except for giant cell arteritis, ocular and systemic risk factors and associated disorders are similar to those described in older AION patients. Younger AION patients have better visual acuity outcomes but a higher risk of fellow eye involvement than older AION patients. (*Am J Ophthalmol* 2007;144:953-960. © 2007 by Elsevier Inc. All rights reserved.)

ANTERIOR ISCHEMIC OPTIC NEUROPATHY (AION), presumably the result of hypoperfusion and infarction of the anterior optic nerve,¹ typically occurs after the age of 55 years. The annual incidence of the nonarteritic form of AION (NAION) is estimated at 2.3 to 10.2 per 100,000 persons aged 50 years and older^{2,3} and at 0.54 per 100,000 for all ages.³ Many previous studies of

NAION, including the multicenter Ischemic Optic Neuropathy Decompression Trial (IONDT), have excluded patients younger than 50 years because of the presumption that NAION is a rare entity in younger patients.⁴⁻⁶

It has been suggested that when AION occurs in a young patient, it is often the result of an underlying condition predisposing the patient to vascular insufficiency, such as diabetes mellitus,⁷ accelerated hypertension,⁸ end-stage renal disease with dialysis,^{9,10} hypotension,⁹ or anemia.⁹ In patients younger than 50 years, diabetes, hypertension, and hypercholesterolemia are associated more strongly with AION than in older individuals.^{11,12} Perioperative ischemic optic neuropathy^{13,14} or AION secondary to hypercoagulable states¹⁵ also have been described in young patients.

Most AION series of younger patients are small,^{11,16-20} and relatively little is known about this group of patients. The aim of our study was to evaluate the characteristics of a large cohort of AION patients younger than 50 years.

METHODS

MEDICAL RECORDS OF ALL PATIENTS WITH AION SEEN IN the Neuro-Ophthalmology Unit at Emory University between 1989 and 2006 were reviewed. Diagnosis of AION was made by two experienced neuro-ophthalmologists (N.J.N. and V.B.) according to the following criteria: 1) a history of sudden or rapidly progressive visual loss secondary to an optic neuropathy; 2) documentation of optic disk edema at the time of visual loss; 3) no evidence of another neurologic or ocular disorder that may be responsible for optic disk edema and visual impairment; and 4) specific exclusion of other causes of optic neuropathy, especially inflammatory optic neuritis by lack of pain on eye movement, lack of substantial improvement on follow-up, and lack of optic nerve enhancement on neuroimaging. Only patients younger than 50 years at the time of initial visual loss were included in our study.

All patients were evaluated in a standard fashion and underwent a systematic comprehensive neuro-ophthalmic history and examination, including dilated funduscopic examination, color fundus photographs, and formal visual field testing by Goldmann perimetry (Haag-Streit, Koeniz, Switzerland) or Humphrey Automated Field Analyzer 24-2 (Carl Zeiss Meditec, Dublin, California, USA). All patients with suspected AION, but aged younger than 50

Accepted for publication Jul 24, 2007.

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TABLE 1. Frequency of Nonarteritic Anterior Ischemic Optic Neuropathy in the Young in Large Series

	Present Study	Hayreh and Associates ^{20*}	Hayreh and Associates ^{11*}	Sawle and Associates ¹⁹	Beri and Associates ^{18*}	Guyer and Associates ¹⁷	Boghen & Glaser ¹⁶
Year published	2007	2001	1994	1990	1987	1985	1975
No. of patients	727	594	406	71	388	200	37
Age range (yrs)	13 to 98	NA	11 to 91	26 to 83	12 to 92	19 to 90	40 to 80
Young NAION							
Age (yrs)	<50	<45	<45	<45	<45	<50	<50
Number of patients (%)	169 (23.2)	108 (14.8)	74 (12.5)	43 (10.6)	3 (4.2)	43 (11.1)	4 (10.8)
Bilateral involvement (%)	70 (41.4)	45 (41.7)	41 (55.4)	17 (39.5)	NA	NA	NA

NA = data not available; NAION = nonarteritic anterior ischemic optic neuropathy.
 Only studies providing the number of patients younger than 50 years with NAION are presented.
 *These series include many of the same patients seen at the University of Iowa.

years, underwent a thorough work-up evaluating for other causes of optic neuropathy, including blood tests and neuroimaging. As soon as the diagnosis of AION was confirmed, all younger patients were evaluated for underlying vascular risk factors, systemic vasculitis, and hypercoagulable states.

Demographic data, ocular characteristics, systemic and ocular risk factors, second eye involvement, recurrence in the same eye, and visual outcome were recorded. The presence of the following potential risk factors was recorded from the medical records: vascular risk factors (diabetes, hypertension, hyperlipidemia, obesity, and tobacco use), other systemic disorders (anemia [hematocrit < 32%], hypotension, blood loss, recent surgical procedure, dialysis, vasculitis, hypercoagulable state, known sleep apnea syndrome), and medications. In addition, ocular risk factors, including cup-to-disk ratio in the affected eye and in the fellow eye, papilledema, and optic nerve head drusen, also were recorded. Visual field defects were classified by their predominant pattern, and severity was rated on a 0-to-3 scale (0, normal; 1, superior or inferior arcuate defect; 2, superior or inferior altitudinal defect; 3, combined superior and inferior defect) to determine the degree of improvement, worsening, or stability. The results of follow-up examinations were recorded when available. Ocular risk factors, visual acuities, color vision score, and perimetry data were derived from all affected eyes (first eyes and subsequently involved fellow eyes). Recurrence was defined as another episode of AION in the same eye after resolution of disk edema. Cup-to-disk ratio analyses were based on that of the fellow eye as previously described.⁶

Statistics were analyzed using SPSS software version 15.0 (SPSS, Inc, Chicago, Illinois, USA). All tests were two tailed, and significance was set at .05. The Mann-Whitney *U* test was used for nonnormal continuous variable comparisons. The Pearson Chi-square test with Yates continuity correction or the Fisher exact test, as appropriate, were used for frequency distribution comparisons. Kaplan-Meier survival analysis was performed to

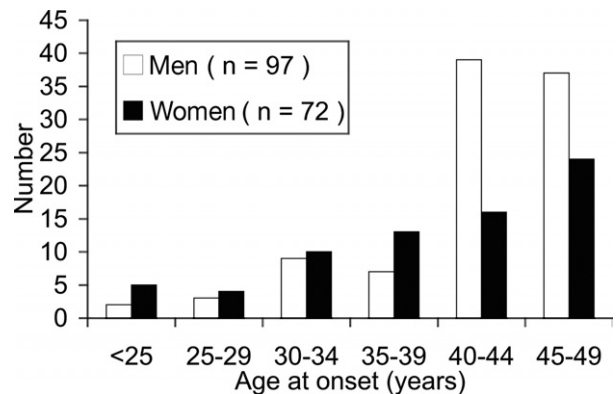


FIGURE. Bar graph showing the distribution of age and gender in 169 young patients with anterior ischemic optic neuropathy.

evaluate the time to involvement of the fellow eye affected by risk factors. Post hoc subgroup analyses regarding gender, race, hypertension, diabetes, tobacco use, alcohol use, sleep apnea, anemia, hypotension, recent operations, dialysis, disk anomaly, dyslipidemia, ischemic heart disease, bilaterality, recurrence, progression, or visual outcome were performed comparing the following groups: age younger than 45 years vs age 45 to 49 years, age younger than 40 years vs age 40 to 49 years, and follow-up of less than six months vs follow-up of six months or more. Benjamani-Hochberg multiple testing correction was applied to these subgroup analyses.

RESULTS

• **DEMOGRAPHICS:** Among the 727 consecutive patients with AION seen in our unit between 1989 and 2006, 169 patients (23%) were younger than 50 years and were included in our study (Table 1). Ninety-nine patients (59%) had unilateral involvement and 70 patients (41%) had bilateral involvement; therefore, analyses were conducted on 239 eyes. There were 98 men (58%) and 71

TABLE 2. Systemic Risk Factors in Patients with Anterior Ischemic Optic Neuropathy in Large Published Series

	Present Study	IONDT ⁴	Hayreh and Associates ¹¹	Hayreh and Associates ¹¹	Guyer and Associates ¹⁷	Repka and Associates ⁵
Age (yrs)	<50	≥50	<45	≥45	17 to 90	≥45
No. of patients	169	420	43	363	200	169
Cardiovascular diseases						
Arterial hypertension	59 (35%)	196 (47%)	11 (26%)	162 (45%)	72 (34%)	65 (38%)
Ischemic heart disease	10 (6%)	46 (11%)	1 (2%)	62 (17%)	—	26 (15%)
Diabetes mellitus	35 (21%)	100 (24%)	9 (21%)	84 (23%)	21 (10%)	26 (15%)
Type 1	10 (6%)	—	6 (14%)	6 (2%)	—	—
Type 2	25 (15%)	—	3 (7%)	78 (21%)	—	—
Hypertension and diabetes mellitus	22 (13%)	—	2 (5%)	49 (13%)	14 (6.6%)	—
Cerebrovascular diseases	2 (1%)	—	1 (2%)	15 (4%)	—	5 (3%)
Hyperlipidemia	39 (23%)	—	11 (26%)	131 (36%)	—	—
Hypercholesterolemia	34 (20%)	—	—	—	—	—
Hypertriglyceridemia	5 (3%)	—	—	—	—	—
Smoking						
Smoked before onset	49 (29%)	—	20 (47%)	187 (52%)	—	—
Average pack-years	20	—	24.8	—	—	—
Still smoking at onset	35 (21%)	—	14 (33%)	92 (25%)	—	—
Anemia	11 (7%)	—	5 (12%)	39 (11%)	—	—
Renal diseases						
Chronic renal failure	8 (5%)	—	1 (2%)	7 (2%)	—	—
Dialysis	8 (5%)	—	—	4 (1%)	—	—
Systemic vasculitides						
Rheumatoid arthritis	3 (2%)	—	—	5 (1%)	—	—
Systemic lupus erythematosus	—	—	1 (2%)	4 (1%)	—	—
Wegener granulomatosis	1 (0.6%)	—	—	—	—	—
Sleep apnea	6 (4%)	—	—	—	—	—
Perioperative AION	9 (5%)	—	1 (2%)	54 (15%)	—	—

AION = arteritic anterior ischemic optic neuropathy; IONDT = Ischemic Optic Neuropathy Decompression Trial; — = data not available.

TABLE 3. Comparison of Studies Detailing Bilateral Nonarteritic Anterior Ischemic Optic Neuropathy

	Present Study	IONDT ³⁰	Kupersmith and Associates ³²	Beck and Associates ³³	Boone and Associates ³¹	Sawle and Associates ¹⁹	Boghen & Glaser ¹⁶
Year published	2007	2002	1997	1997	1996	1990	1975
No. of patients	169	418	100	643	99	71	37
Age range (yrs)	13 to 49	50 to 89	>49	NA	39 to 90	26 to 83	40 to 80
No. with bilateral ON at baseline	17 (10%)	88 (21%)	15 (15%)	154 (24%)	6 (6%)	3 (4%)	13 (35%)
No. with bilateral ON at follow-up	70 (41%)	140 (33%)	33 (33%)	202 (31%)	23 (23%)	20 (28%)	14 (38%)
Median/mean duration of follow-up	Seven mos/23 mos	Median, 5.1 yrs	NA	NA	NA	Mean, 5.3 yrs	NA
Range of follow-up duration (yrs)	1 to 21	0 to 7.4	≥2	0 to ≥5	≥3.5	NA	93% ≥ 3; 79% ≥ 5

IONDT = Ischemic Optic Neuropathy Decompression Trial; NA = data not available; ON = optic neuropathy.

women (42%), aged 13 to 49 years (median, 43 years; Figure 1). Women had their first onset of AION at a significantly younger age than men (median age, 41 and 43 years for women and men, respectively; $P = .05$). One

hundred and fifty-seven patients (93%) were White, nine were Black, one was Indian, and two were of Other races. Four patients had a history of AION before the age of 50 years in their families.

TABLE 4. Comparison of Risk Factors in Unilateral and Bilateral Cases of Anterior Ischemic Optic Neuropathy in the Present Series

	Unilateral	Bilateral	Total
No. of patients	99	70	169
No. of eyes	99	140	239
Patient characteristics			
Gender			
Male	61 (62%)	37 (53%)	98 (58%)
Female	38 (38%)	33 (47%)	71 (42%)
Age at onset (yrs)			
Range	13 to 49	18 to 49	13 to 49
Median	43	42	43
Systemic risk factors			
Arterial hypertension	30 (30%)	29 (41%)	59 (35%)
Ischemic heart disease	3 (3%)	7 (10%)	10 (6%)
Diabetes mellitus	17 (17%)	18 (26%)	35 (21%)
Type 1	3 (3%)	7 (10%)	10 (6%)
Type 2	14 (14%)	11 (16%)	25 (15%)
Hypertension and diabetes mellitus			
Cerebrovascular disease	1 (1%)	1 (1.4%)	2 (1%)
Hyperlipidemia	21 (21%)	18 (26%)	39 (23%)
Hypercholesterolemia	19 (19%)	15 (21%)	34 (20%)
Hypertriglyceridemia	2 (2%)	3 (4%)	5 (3%)
Tobacco use	28 (28%)	21 (30%)	49 (29%)
Anemia	1 (1%)	10 (14%)	11 (7%)
Renal diseases			
Chronic renal failure	2 (2%)	6 (9%)	8 (5%)
Dialysis	2 (2%)	6 (9%)	8 (5%)
Systemic vasculitides			
Rheumatoid arthritis	2 (2%)	1 (1.4%)	3 (2%)
Wegener			
granulomatosis	1 (1%)	0	1 (0.6%)
Sleep apnea	3 (3%)	3 (3%)	6 (4%)
Perioperative	4 (4%)	5 (7%)	9 (5%)
Ocular risk factors (eyes)			
Crowded disk	83 (83%)	106 (76%)	189 (82%)
Papilledema	2 (2%)	6 (4%)	8 (3.5%)
Drusen	6 (6%)	7 (5%)	13 (6%)

• **ASSOCIATED RISK FACTORS:** Seventy-four percent of patients (125/169) had at least one concurrent or preexisting systemic risk factor (Table 2). Thirty-five percent of patients had arterial hypertension, 21% had diabetes mellitus, and 13% had both arterial hypertension and diabetes mellitus. Of 35 patients with diabetes mellitus, 29% were type I and 71% were type II. Twenty-three percent of patients had dyslipidemia by history or laboratory testing and 20% were obese. Twenty-one percent of patients currently smoked cigarettes and 8% reported previous cigarette use. Six percent of patients had ischemic heart disease and 1% had previous stroke. Seven percent of patients had anemia, 5% were undergoing renal dialysis, and 4% had known sleep apnea. A hypercoagulable state was demonstrated in nine patients (5%), including three

cases of hyperhomocysteinemia, one case of heterozygosity for the methyltetrahydrofolate reductase (*MTHFR*) gene, and five cases of antiphospholipid antibodies. There were four patients (2%) who had systemic vasculitis that might have predisposed them to development of AION, including three cases of rheumatoid arthritis and one case of Wegener granulomatosis.

Perioperative AION occurred in nine cases (5%) and included those undergoing cardiac surgery (four cases), spine surgery (one case), gynecologic surgery (two cases), and hip surgery (one case). One patient had AION during cataract surgery. Four patients were taking medications potentially associated with AION including amiodarone, sildenafil, and oxymetazoline nasal spray.

The details of cup-to-disk ratio and optic nerve head anomalies were available for 230 eyes. Ninety-two percent (210/230) of eyes had an underlying small or anomalous optic disk. One hundred and eighty-nine eyes (82%) had small physiologic cups (cup-to-disk ratio less than 0.2), 13 eyes (6%) had optic disk drusen, and eight eyes (4%) had papilledema. Twenty-six percent of patients (44/169) had isolated disk anomalies without any systemic risk factors. Twenty eyes of 15 patients had no disk anomalies, including no small physiologic cup. These 15 patients had at least one systemic risk factor, including arterial hypertension (n = 5), diabetes mellitus (n = 4), tobacco use (n = 6), obesity (n = 3), renal dialysis (n = 2), dyslipidemia (n = 2), anemia (n = 3), perioperative state (n = 2), and antiphospholipid antibodies (n = 1).

• **FELLOW EYE INVOLVEMENT:** Follow-up information was available for 164 patients. The median follow-up period after onset in the first affected eye was seven months (range, one to 252 months; semi-interquartile range, 10 months). There were no differences between patients with fewer than six months of follow-up compared with those with more than six months follow-up, except that the frequency of bilaterality was more common in those with more than six months of follow-up (53% vs 25%; *P* = .01).

Of the 99 patients with unilateral involvement, the right eye was involved in 49% of patients and the left eye was involved in 51%. Of the 70 patients with bilateral optic neuropathy (Table 3), nine patients (13%) already had optic nerve pallor and abnormal visual fields in their fellow eye at presentation (presumably representing previous asymptomatic involvement), eight patients (11%) had simultaneous binocular involvement, and 53 patients (76%) had acute disease in one eye followed by sequential second eye involvement during follow-up. Among the 53 patients with observed sequential second eye involvement, the median time between involvement of the two eyes was 12 months (range, one week to 168 months).

The local and systemic risk factors in unilateral and bilateral cases of young AION in our series are detailed in Table 4. Anemia was the only systemic risk factor significantly more prevalent among bilaterally affected patients

compared with unilateral patients (16% vs 1%; $P = .0003$). Kaplan-Meier survival analysis was performed to determine if hypertension, smoking, diabetes, dyslipidemia, anemia, or obesity affected the timing of fellow eye involvement. Anemia ($P < .001$) and type 1 diabetes ($P = .01$) showed a significant decrease in time to fellow eye involvement. Ten of the 11 patients with anemia had fellow eye involvement during follow-up (median, nine weeks; range, one to 72 weeks), and seven of the 10 patients with type 1 diabetes ultimately had fellow eye involvement (median, 16.5 weeks; range, two to 96 weeks).

Among the eight cases with bilateral simultaneous AION, seven (88%) had events with documented or presumed blood pressure fluctuations (three with cardiac surgery; one each with Caesarean section with hypotension, hypotension during dialysis, malignant hypertension, and severe gastrointestinal bleeding). Three of these patients had coexisting anemia. The eighth patient had type 1 diabetes.

• **RECURRENCE IN THE SAME EYE:** Eleven eyes of 10 patients (6%) experienced a recurrence of AION in the same eye. The interval between the first and second episodes ranged from two months to 21 years. There was no significant association between recurrence of AION in the same eye and systemic risk factors.

• **VISUAL FUNCTION AT INITIAL PRESENTATION AND AT FOLLOW-UP:** Initial visual acuities in all affected eyes ranged from 20/15 to light perception, with a median of 20/30. At initial presentation, 59% (141/226) of the eyes had a visual acuity of 20/40 or better and 20% (46/226) had a visual acuity of 20/200 or worse. At last follow-up, visual acuity was 20/40 or better in 64% (146/229) and 20/200 or worse in 22% (51/229). Compared with the initial examination, 85 of 215 eyes (40%) showed no change, 74 eyes (34%) showed improvement of 1 line or more, and 56 eyes (26%) showed worsening by 1 or more lines. There was no significant difference between initial and final median visual acuity. Analysis of the 70 patients with bilateral NAION showed that visual acuity in the first and second affected eyes differed by 1 line or fewer (Early Treatment of Diabetic Retinopathy equivalent) in 36% of patients and 3 lines or fewer in 70% of patients.

The median Ishihara plate color vision score for the first eye affected with NAION was 13 of 14 and for the second affected eye was 12 of 14. Initial visual field testing showed a marked prevalence of inferior visual field defects. The most frequent defects were inferior altitudinal (39%), followed by coexisting superior and inferior arcuate (15%), inferior quadrantanopia (12%), inferior arcuate (9%), and superior altitudinal (8%). At the last follow-up, 148 (72%) of 206 eyes showed no change in severity of visual field defects, 16 eyes (8%) showed improvement, and 42 eyes (20%) showed worsening.

• **THE EFFECTS OF AGE:** There were no significant differences between patients younger than 45 years and those 45 to 50 years of age. However, because we suspected patients younger than 40 years also may represent a different subcategory (see Figure 1), we performed a post hoc subanalysis on this group. Patients younger than 40 years were significantly more likely to be women (58% vs 34%; $P = .03$), were less likely to have dyslipidemia (8% vs 29%; $P = .03$), and had better visual field outcomes ($P = .03$). These patients had a trend toward significantly less hypertension ($P = .051$) and type 2 diabetes ($P = .051$) compared with older patients. However, the frequency of one or more vascular risk factors was similar in both groups (58% of the patients younger than 40 years vs 67% of patients older than 40 years; $P = .27$).

DISCUSSION

AION IS THE MOST FREQUENT ACUTE OPTIC NEUROPATHY in patients older than 50 years. Although AION is less common in younger patients, it is by no means rare. Several large series have reported that 10.5% to 12.5% of AION patients are younger than 45 years (Table 1).^{11,17,18,20} Our study confirmed that AION in the young is not uncommon and represents 23% of AION patients younger than 50 years and 15% of AION patients younger than 45 years in a tertiary neuro-ophthalmic service. Ninety-three percent of our younger AION patients were white, a proportion similar to the 95% of patients reported in the IONDT and other studies of NAION patients of all ages.^{4,11,17} The slight predominance of males in our study was similar to the IONDT's cohort of older NAION patients.⁴ However, in our patients younger than 40 years, females were affected more frequently than males (Figure 1).

NAION has been reported to be associated with many conditions that may predispose to decreased optic nerve head perfusion (Table 2).²¹⁻²⁴ If one includes only systemic factors considered in the IONDT, 66% of our patients younger than 50 years and 58% of our patients younger than 40 years had one or more vascular risk factors thought to be associated with small-vessel cerebrovascular disease, including hypertension, diabetes mellitus, hypercholesterolemia, obesity, and cigarette use. These percentages are comparable with the 60% of patients reported by the IONDT.⁴

In a few prior series, hypertension and diabetes were associated strongly with the development of NAION, especially at a younger age (Table 2).^{5,11,17} Thirty-five percent of our patients had systemic hypertension, compared with 34% to 47% in other studies,^{4,5,11,17} and 21% of our patients had diabetes mellitus, compared with 10% to 24% in other studies.^{4,5,11,17} Some investigators have claimed an association between NAION and other cardiovascular diseases such as stroke and ischemic heart disease using general population studies as controls.^{11,17} The

prevalence of these conditions among our patients was relatively low compared with older individuals in other studies, but the prevalence of ischemic heart disease is approximately 1%, and the prevalence of stroke is approximately 0.4% among persons younger than 45 years in the United States.²⁵ Thus, if one compares the risk of ischemic heart disease and stroke found in our study to a similarly aged population, our young NAION patients were affected by these conditions more frequently. Although the inclusion of patients 45 to 49 years of age makes it more difficult to compare our data with those of prior series that used an age cut-off of 45 years and potentially might have overestimated the frequency of vascular risk factors, we included these patients to provide data that we could compare directly with those of the IONDT, which studied only patients 50 years of age and older. In addition, subgroup analyses found no differences among the patients 45 to 49 years of age, suggesting that including them does not substantially alter the conclusions regarding risk factors. In fact, even most patients younger than 40 years had one or more vascular risk factors.

Our study also showed that optic disk structure likely plays an important role in the development of AION in younger patients, similar to studies of older NAION patients in which cupless or small optic nerves were noted in 97% to 98% of cases.^{6,26} Eighty-two percent of our patients had a small or no physiologic cup, the so-called disk at risk. Optic disk drusen, which represents another crowded optic disk anomaly that previously was associated with a younger age of onset of NAION,²⁷ was found in 6% of our patients. Twenty-six percent of our patients had only optic disk anomalies without any known systemic risk factors, suggesting that optic nerve head structure alone may be sufficient to cause this disease even in younger patients.

Besides local anatomic and systemic hemodynamic factors, thrombophilic factors also may contribute to the pathogenesis of NAION. Many prothrombotic states, including antiphospholipid antibodies, protein C and S deficiency, antithrombin deficiency, tissue plasminogen activator deficiency, hyperhomocysteinemia, heterozygous factor V Leiden mutation, and *MTHFR* mutations have been demonstrated in patients with NAION.^{15,22,28,29} Although these factors were not a prominent feature in our series, we recommend that laboratory testing be carried out to exclude thrombophilic factors, especially those without conventional vascular risk factors. Furthermore, it is particularly important to exclude them in patients without a small cup-to-disk ratio or other disk anomaly at presentation, because all such patients in our study were found to have some underlying vascular risk factor. Indeed, because of the retrospective nature of our study, we likely underestimated some of these thrombophilic factors. The battery of tests undergone by our patients varied over time based on the availability of some tests and was more extensive after the mid-1990s.

The risk of second eye involvement in patients older than 50 years with NAION in the IONDT was approximately 15% within five years and was related to poor baseline visual acuity in the first eye and to diabetes mellitus, but not to age, gender, smoking history, or aspirin use.³⁰ Our data indicate that young AION patients may have a higher risk of fellow eye involvement than older AION patients. In our study, 53 (35%) of the 152 patients who had monocular disease at presentation had subsequent involvement of the second eye at a median follow-up of only seven months. In addition, our rate of bilateral involvement at last follow-up was more than the range of 23% to 38% observed in other series of mostly older patients with NAION (Table 4).^{16,19,30-33} This increased rate of bilaterality also was found among the younger patients in the Iowa cohort (Table 1),^{11,20} but it is possible these findings reflect a referral bias of more severely affected cases to tertiary level services.

In our study, anemia was more frequent among patients with bilateral disease than unilateral disease (Table 3), and both anemia and type 1 diabetes mellitus were significantly associated with decreased time to second eye involvement. In the significant majority of patients with bilateral sequential AION, visual acuity was similar between the first and fellow eyes at follow-up.

Bilateral simultaneous involvement by AION was related primarily to severe blood pressure fluctuations (either hypotension or hypertension), typically seen during surgery or in the setting of dialysis. One patient with type 1 diabetes mellitus had bilateral simultaneous AION. Indeed, our patients with sequential AION and type 1 diabetes mellitus had second eye involvement as early as two weeks, emphasizing that type 1 diabetes is an important risk factor for the rapid development of bilateral AION among younger patients.

Recurrence of NAION in the affected eye is unusual. Hayreh and associates reported recurrent episodes in only 45 of 594 patients (7.5%), and the greatest number of patients with recurrence were 45 to 64 years of age.²⁰ In our study, 11 eyes (4.6%) of 10 patients (6%) had more than one episode of AION in the same eye. Similar to cases with recurrent NAION in the young reported in the literature,^{7,34-37} all patients in our series also had bilateral sequential NAION. In only one patient did more than one recurrence of NAION develop in both eyes, resulting in severe visual loss in both eyes. We found no association between systemic conditions and recurrence of AION in our patients.

Our data show young patients with AION have better visual acuity outcomes than those reported in older patients with AION. In the IONDT, 35% of affected eyes had visual acuity better than 20/64 and 36% had visual acuity worse than 20/200,⁴ whereas among our young patients with AION, 73% had visual acuity better than 20/64 and only 18% had visual acuity worse than 20/200. These findings support a trend of significantly better visual

outcomes in younger patients affected by AION that was found in both the IONDT and another study of primarily older patients with AION.^{4,38}

Several limitations of the present study should be addressed, most of which relate to the nature of large retrospective analyses. First, existing medical diagnoses often were made by patient report, not by strict assessment of medical data. For example, we did not systematically study sleep apnea by polysomnography, although all patients were questioned about a medical diagnosis of sleep apnea. Similarly, given that our study encompasses a 17-year period, there were obviously changes in the panel of hypercoagulation studies and neuroimaging protocols, but the best techniques available at our institution were applied in each case. Finally, not all our patients had the same extent of follow-up, but there was no difference between those patients followed up for more than six months compared with those followed up for fewer, except for a higher rate of bilaterality among the former. This is

not surprising given that patients with involvement of their second eye would be more likely to seek treatment from us again for their new symptoms, and we typically follow-up patients with bilateral involvement more closely for longer periods. Regardless, if we underestimated the rate of bilaterality, this would only strengthen our conclusion that bilaterality is more frequent among younger patients.

In conclusion, AION in younger patients is not rare, representing 23% of all patients with AION in our tertiary neuro-ophthalmic service. We found AION in younger patients to be similar in many ways to NAION as described in older patients, with the exception of better visual acuity outcomes and a higher propensity for bilateral involvement. AION should be considered in the differential diagnosis of younger patients with a painless optic neuropathy with disk edema at presentation, and these patients require a thorough systemic evaluation for underlying vascular risk factors.

THIS STUDY WAS SUPPORTED IN PART BY A GRANT TO THE DEPARTMENT OF OPHTHALMOLOGY FROM RESEARCH TO Prevent Blindness, Inc, New York, New York, and by core Grant P30-EY06360 to the Department of Ophthalmology from the National Institutes of Health, Bethesda, Maryland. Dr Newman is a recipient of a Research to Prevent Blindness Lew R. Wasserman Merit Award. Involved in design of study (V.B., N.N.); conduct of study (P.P., B.B.B., N.N., V.B.); statistical analysis (B.B.B., P.P.); and preparation and review of manuscript (P.P., B.B.B., N.N., V.B.). The study was approved by Emory University's Institutional Review Board.

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