Optic Nerve Decompression Surgery for Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) Is Not Effective and May Be Harmful

The Ischemic Optic Neuropathy Decompression Trial Research Group

Objective.—To assess the safety and efficacy of optic nerve decompression surgery compared with careful follow-up alone in patients with nonarteritic anterior ischemic optic neuropathy (NAION).

Design.—The Ischemic Optic Neuropathy Decompression Trial (IONDT) is a randomized, single-masked, multicenter trial.

Setting.—Twenty-five US clinical centers.

Participants.—The IONDT ceased recruitment on October 20, 1994, on the recommendation of its Data and Safety Monitoring Committee. The preliminary results presented herein are based on data as of September 8, 1994, from 244 patients with NAION and visual acuity of 20/64 or worse. One hundred twenty-five patients had been randomized to careful follow-up, and 119 had been randomized to surgery, with 91 and 95, respectively, having completed 6 months of follow-up.

Intervention.—Patients in the surgery group received optic nerve decompression surgery and follow-up ophthalmologic examinations; those in the careful follow-up group received ophthalmologic examinations at the same times as the surgery group.

Main Outcome Measures.—Gain or loss of three or more lines of visual acuity on the New York Lighthouse chart at 6 months after randomization, as measured by a technician masked to treatment assignment.

Results.—Patients assigned to surgery did no better when compared with patients assigned to careful follow-up regarding improved visual acuity of three or more lines at 6 months: 32.6% of the surgery group improved compared with 42.7% of the careful follow-up group. The odds ratio (OR) for three or more lines better, adjusted for baseline visual acuity and diabetes, was 0.74 (95% confidence interval [CI], 0.39 to 1.38). Patients receiving surgery had a significantly greater risk of losing three or more lines of vision at 6 months: 23.9% in the surgery group worsened compared with 12.4% in the careful follow-up group. The 6-month adjusted OR for three or more lines worse was 1.96 (95% CI, 0.87 to 4.41). No difference in treatment effect was observed between patients with progressive NAION and all others.

Conclusion.—Results from the IONDT indicate that optic nerve decompression surgery for NAION is not effective, may be harmful, and should be abandoned. The spontaneous improvement rate is better than previously reported.

(*JAMA*. 1995;273:625-632)

From the Ischemic Optic Neuropathy Decompression Trial Research Group.

The major participants in the Ischemic Optic Neuropathy Decompression Trial are listed at the end of this article.

Reprint requests to the Department of Ophthalmology, University of Maryland School of Medicine, 419 W Redwood St, Baltimore, MD 21201 (Shalom Kelman, MD).

NONARTERITIC anterior ischemic optic neuropathy (NAION) is the most common cause of acute optic nerve disease in the elderly[1-3] and often results in severe visual loss. Estimates of the number of new cases seen each year in the United States range from approximately 1500[4] to 6000.[5] Clinically, NAION is characterized by sudden and painless loss of vision in one eye associated with pallid swelling of the optic disc. Although nonarteritic ischemic optic neuropathy can be caused by giant cell arteritis and is thought by many to be due to microvascular occlusive disease, its etiology is unknown. Anatomical factors appear to contribute to the vascular event initiating NAION, as the number of patients with NAION who congenitally lack a physiological cup in their optic discs is greater than expected. Visual function may be impaired through decreased central visual acuity, peripheral visual field loss, or both. Because NAION can eventually affect both eyes in up to 40% of patients,[6] it is believed to take a devastating toll on independence and quality of life. In addition, the literature has supported the notion that final visual acuity in patients with NAION declines to 20/200 or worse in about 45% of affected eyes.[7,8]

For editorial comment see p 666.

Until recently, the clinician's main task in managing patients with NAION was to exclude temporal arteritis (which is treatable with corticosteroids) and to control other factors, such as elevated blood pressure, which might affect the final visual outcome. Although various nonsurgical treatments, such as corticosteroids and phenytoin sodium, have been tried, no therapy for NAION has been proven effective.

In 1989,[9] it was first suggested that optic nerve decompression surgery (ONDS) might improve vision, particularly in patients with a progressive form of NAION characterized by a worsening of visual acuity during a period of

days or weeks. The surgery involves making two or more slits or a window in the optic nerve sheath, allowing cerebrospinal fluid to escape, thereby reducing the pressure surrounding the optic nerve. Other investigators[10-12] subsequently reported a beneficial effect of ONDS on visual acuity and visual fields, and the observed effect on visual acuity was not always limited to patients with progressive disease.

None of the studies reporting improvement[9-12] was a randomized controlled trial. Furthermore, sample sizes were generally small, uniform visual testing procedures were not used, and progressive disease was not well defined. As surgery was being performed more frequently, it became imperative to test the procedure in a randomized clinical trial before widespread use. Accordingly, the Ischemic Optic Neuropathy Decompression Trial (IONDT) was initiated.

METHODS

The IONDT is a multicenter randomized controlled clinical trial sponsored by the National Eye Institute. The objective of the IONDT is to assess the safety and efficacy of ONDS and follow-up compared with careful follow-up alone, in patients with NAION.

Eligibility and Enrollment

Patients were eligible for randomization if they were diagnosed by a study neuro-ophthalmologist as having NAION. Criteria for eligibility were determined before the study start and were applied according to protocol by the study neuro-ophthalmologist and other certified study staff, where appropriate. They included sudden onset of subjective symptoms of loss of vision; a best-corrected visual acuity in the affected eye of 20/64 or worse; a relative afferent pupillary defect (bilateral disease excepted); optic disc edema; and visual field defects consistent with optic neuropathy. Study-specific criteria included age 50 years or older, duration of symptoms less than 14 days at the baseline examination, and the patient being able and willing to give informed consent.

Medical exclusion criteria included conditions likely to exclude NAION as the primary diagnosis: evidence of temporal arteritis, such as Westergren sedimentation rate greater than 40 mm/h, or a history of optic neuritis, multiple sclerosis, collagen vascular disease, or other inflammatory disease. Patients also were excluded if they had a condition putting them at increased surgical risk: intolerance of or allergy to inhalational anesthetics, myocardial infarction within the previous 6 months, current anticoagulation therapy that could not be stopped, or an abnormal platelet count or hematocrit.

Ophthalmologic exclusion criteria included conditions that indicated a nonischemic etiology, such as vitreous hemorrhage or cells, iritis, pain on eye movement characteristic of optic neuritis, cataract surgery within 3 months, or prior eye surgery. Exclusions also included other ophthalmologic conditions that might impair a measurement of change in visual acuity or visual field, including lens opacity, macular disease, visually significant retinopathy, glaucoma or intraocular pressure greater than 30 mm Hg, or other progressive eye disease. Also excluded were patients who had NAION occurring in the other eye within 14 days of the onset of the current symptoms, visual acuity of no light perception, continued use of drugs known to affect the optic nerve or retina, or any factor likely to deter the patients from returning for follow-up visits.

Patients eligible for randomization by all criteria, except that their visual acuity was better than 20/64 at the baseline examination, had an opportunity to participate in the trial if their vision deteriorated to 20/64 or worse within 30 days from the onset of symptoms. Visual acuity was measured weekly until 30 days from symptom onset had passed or the vision criterion was met. This group of patients whose vision deteriorated to 20/64 within 30 days was termed the late-entry group. Randomized patients who were not late entry were termed the regular-entry group.

Patients were referred to the trial for eligibility screening by vision care specialists in the surrounding communities. Clinic coordinators conducted a preliminary screening by telephone, and potentially eligible patients were scheduled for a baseline eligibility visit. The baseline eligibility visit consisted of medical history, an ocular/medical examination, measurement of visual acuity, and measurement of visual fields using automated perimetry.

Patients agreeing to participate in the IONDT signed a consent form approved by the local institutional review board and were randomized to one of two groups: ONDS or conventional observational management ("careful follow-up") with no surgical intervention. Consent forms were generally uniform in content and structure across the study clinics but had individual variations as required locally. The randomization schedule was stratified by clinic, with allocations within each clinic balanced across treatment groups using randomly permuted blocks of size two or four, always starting with a block size of two and randomly selecting the size thereafter. Block sizes were unknown to the clinics. The patient became officially enrolled in the trial at the time the clinic coordinator or study neuro-ophthalmologist telephoned the coordinating center and received the randomization assignment.

Patients who were randomized into the ONDS group were required to receive surgery within 4 days of randomization. Surgery had to take place within 14 days of the onset of symptoms (date of onset was day 0) for the regular-entry patients and within 34 days of the onset of symptoms for the late-entry patients. If randomization occurred more than 1 day after the baseline eligibility visit for any patient, the visual acuity and visual fields were retested at randomization and used for the baseline values.

Surgeons were required to have performed 10 or more decompression surgeries to be certified to perform surgery within the IONDT. The surgical procedure was performed by a certified study surgeon according to an explicit study protocol. Surgery was performed under general anesthesia, using a medial approach. Surgeons fenestrated the optic nerve sheath using at least two slits or at least one window. The study surgeon was required to report immediately to the coordinating center any serious complications, including orbital hemorrhage, central retinal artery occlusion, or no light perception vision immediately following surgery.

Outcome and Other Measures

The primary outcome for the IONDT, specified before the study start, was an improvement (from randomization) of three lines or more of visual acuity, measured using the New York Lighthouse charts (Lighthouse Low Vision Products, Long Island City, NY), 6 months after randomization. This outcome was also measured at 3 months, 12 months, and every 6 months subsequently. A worsening by three lines or more of visual acuity at the same follow-up points was used as the principal measure of safety.

Visual acuity scores were converted to log MAR (log of the minimum angle of resolution)[13] (Table 1) using the following formula: log MAR=1.70−0.02N, where N is the number of letters read on the vision chart; a decrease of 0.3 log MAR corresponds to three lines better on the Lighthouse chart. For the purposes of our analysis, each incrementally worse level of "off-the-chart" vision was assigned a value 0.30 log MAR units higher: count fingers=2.0 log MAR; hand motion=2.3 log MAR; light perception=2.6 log MAR; and no light perception=2.9 log MAR. This approach is

Table 1.—Snellen Visual Acuity and Log of the Minimum Angle of Resolution (Log MAR) Equivalents

Visual Acuity Equivalents		
Snellen Feet	Visual Acuity Score, *N*	Log MAR*
20/10	100	−0.30
20/15	91	−0.12
20/20	85	0
20/25	80	+0.10
20/30	76	+0.18
20/40	70	+0.30
20/50	65	+0.40
20/60	61	+0.48
20/64	60	+0.50
20/70	58	+0.54
20/80	55	+0.60
20/100	50	+0.70
20/200	35	+1.0
20/300	26	+1.18
20/400	20	+1.30
20/800	5	+1.60
20/1000	0	+1.70
Count fingers	0	+2.00
Hand motion	0	+2.30
Light perception	0	+2.60
No light perception	0	+2.90

*Log MAR=1.70−0.02*N*, where *N* is the number of letters read on the vision chart.

similar to that used by others.[14]

Additional outcome measures include visual field score mean deviation at 3, 6, and 12 months from Program 24-2 analyzed with StatPac on the Humphrey Field Analyzer; quality of life as measured by the Short-Form Health Survey (SF-36)[15] and an IONDT-specific health-related quality-of-life instrument at 6 and 12 months; occurrence of systemic and ophthalmic intraoperative complications (defined as occurring during surgery) or postoperative complications (defined as occurring in the first postoperative week); and other morbidity or mortality outcomes potentially related to ONDS.

All patients enrolled in the trial were followed up in an identical fashion, regardless of treatment group. Patients were seen for follow-up visits at or about 1 week, 1 month, 3 months, 6 months, and 12 months after randomization, and at 6-month intervals thereafter. Patients were expected to have at least 1 year of follow-up. Visual acuity was measured during visits at 1 week and 1 month after randomization to monitor the safety of the treatment assigned; the protocol did not require that vision at these visits be measured by a masked, certified technician or using a Lighthouse chart. Subsequent measurements were performed at each follow-up visit according to a uniform protocol by an IONDT-certified technician masked to the treatment received.

We operationally defined progressive status in three alternative ways: (1) eligible patients whose vision was better than 20/64 at 14 days from the onset of symptoms of NAION but deteriorated to 20/64 or worse within 30 days (ie, enrollment type was late entry); (2) the subgroup of patients meeting criteria for late entry who lost three or more lines of vision between the baseline eligibility visit and randomization; and (3) all regular- and late-entry patients who reported a subjective worsening of vision between onset of symptoms and the baseline eligibility visit.

We defined surgical experience in three ways. One definition was in relation to the surgeon: number of lifetime decompression surgeries performed (<15 vs ≥15); and two definitions related to clinic experience: (1) clinics with at least one surgeon with 15 or more decompresion surgeries vs all other clinics; and (2) clinics with at least one surgeon with five or more IONDT surgeries who had a low complication rate (20% or fewer intraoperative complications) vs all other clinics. Because the definition related to the surgeon could be applied only to patients having surgery, we only used this definition in examining the association between surgical experience and outcome within the surgery group.

Statistical Analysis

Sample size calculations were based on a two-sided .05 significance level test for comparison of the proportion of patients in the two study groups expected to improve three or more lines of vision. The sample size was determined by specifying that the test have a power of at least 90% to detect a treatment difference between groups, assuming 50% of the surgery patients and 30% of the careful follow-up patients would improve three or more lines of vision during the course of the study. The resulting sample size was calculated as 135 in each group. Allowing for 10% attrition, a total of 150 patients were calculated as needed for each study group.

Patients were analyzed as part of the treatment group to which they were assigned (intention-to-treat analysis). All analyses compare patients randomized to ONDS with those randomized to careful follow-up. For analysis of the visual acuity outcome, patients were classified as (1) getting better (improving three or more lines of vision); (2) little change (increase or decrease of fewer than three lines); or (3) getting worse (worsening by three or more lines) between randomization and the specified follow-up visit.

For the measure of treatment effect, we used relative risks (RRs) instead of odds ratios (ORs) because RRs are directly interpretable as ratios of risks. In most analyses we report two sets of RRs, comparing the surgery group with the careful follow-up group on getting better and getting worse. An RR greater than 1.0 for getting better indicates that surgery is more beneficial than careful follow-up; an RR between 0 and 1.0 for getting better indicates that surgery is less beneficial than careful follow-up; and an RR greater than 1.0 for getting worse indicates that surgery is more harmful than careful follow-up. The RRs and 95% confidence intervals (CIs)[16] comparing surgery with careful follow-up for improvement and worsening of visual acuity were estimated at 3, 6, and 12 months of follow-up. The 95% CIs for the RRs that do not include 1.0 correspond to RRs with associated *P* values of less than .05 for a two-sided test of the null hypothesis that the RR equals 1. The *P* values presented herein are for two-sided tests and have not been adjusted for multiple comparisons.

Variables examined for possible interaction or confounding include clinic, sex, patient age (<65 vs ≥65 years), race, progressive status, initial symptoms, days from onset of symptoms to referral, days from onset of symptoms to randomization, hypertension, diabetes, presence of cataract, prior NAION, randomization visual acuity, regular aspirin use, and surgical experience. Particular attention was paid to variables distributed differentially in the two treatment groups at baseline.

Relative risks are reported both as unadjusted and as adjusted across subgroups using the Mantel-Haenszel method. When there was evidence of possible subgroup interaction with treatment group (ie, differential treatment effects in some subgroups), we present RRs separately for these subgroups and do not report an adjusted RR.

To adjust for several variables simultaneously and to evaluate interactions in this setting, we used multiple logistic regression analysis and calculated the ORs as the measure of treatment effect. The OR for getting better (or worse) is defined as the odds of getting better (or worse) among surgery patients divided by the odds of getting better (or worse) among careful follow-up patients. All logistic regression analyses were adjusted for randomization visual acuity. Other variables examined for possible interaction with treatment group and confounding of treatment effect were sex, age, late-entry status, diabetes, and aspirin use. These variables either were distributed differently between the two study groups at randomization ($P<.10$, diabetes and late entry) or had suggested heterogeneity of RRs in strata when examined by the Mantel-Haenszel method ($P<.20$, aspirin, sex, and age). Possible interactions were examined first and were retained in the model when

Table 2.—Expected and Completed Follow-up Visits, by Treatment Group*

	Careful Follow-up, No. (%) (n=125)	Surgery, No. (%) (n=119)
Total expected 3-mo visits	117 (100)	108 (100)
Completed visits	113 (97)	105 (97)
Missed visits	4 (3)	3 (3)
Information not yet received/entered	0	0
Visits not yet expected	8	11
Total expected 6-mo visits	98 (100)	99 (100)
Completed visits	91 (93)	95 (96)
Missed visits	1 (1)	0
Information not yet received/entered	6 (6)	4 (4)
Visits not yet expected	27	20
Total expected 12-mo visits	67 (100)	62 (100)
Completed visits	55 (82)	54 (87)
Missed visits	4 (6)	2 (3)
Information not yet received/entered	8 (12)	6 (10)
Visits not yet expected	58	57

*Data as of September 8, 1994. Total numbers may vary in subsequent tables because of missing values for visits or variables.

the interaction P value was less than or equal to .05. Variables were considered to be confounding if including them in the model changed the estimated treatment effect by 20% or more. In the final analysis, we adjusted for all interactions and confounding variables identified and for any variable having a significant relationship ($P \leq .05$) with the outcome when the interactions and confounding variables were in the model.

Mean deviation of visual field, the secondary outcome, was analyzed as a continuous variable: change from randomization at the 3-, 6-, and 12-month follow-up visits. Using change in mean deviation from randomization to the 6-month visit as the outcome variable, we used multiple linear regression methods to estimate the treatment effect (ie, the mean difference in the response in surgery minus careful follow-up) adjusted for any confounding variables and significant ($P \leq .05$) interactions with treatment effect.

The Data and Safety Monitoring Committee (DSMC) reviewed the accumulated data from the trial at four points (April 1993, October 1993, April 1994, and October 1994). Study personnel caring for patients, including the study chair, did not see the data until after recruitment for the trial had ceased.

RESULTS

Recruitment for the IONDT began in October 1992. The results presented herein are based on data as of September 8, 1994, when 244 patients with NAION had been randomized, 125 to careful follow-up and 119 to surgery (Table 2). These data were presented to the DSMC at their October 19, 1994, meeting and led to their recommendation that recruitment to the IONDT cease and that patients continue to be followed up for at least 1 year. Randomization ceased on October 20, after a total of 258 patients had been randomized. One of the 26 clinical centers was removed from the study in April 1994 because of serious protocol violations; its data, including 21 patients, are not included in the analysis or tables.

Demographic and other characteristics are summarized in Table 3. In general, there were few differences between groups: more patients with diabetes were assigned to the careful follow-up group, and more late-entry patients were assigned to the surgery group.

Misdiagnoses and Adherence

After randomization, two patients were reported to have optic neuritis and one was diagnosed with temporal arteritis (by biopsy), for a total of three misdiagnoses. The results of analyses performed with and without these patients do not differ in any meaningful way.

Three patients assigned to careful follow-up requested surgery after they received their treatment assignment, and two patients assigned to surgery received careful follow-up, one by choice and one because of a newly discovered colon malignancy. Three patients (one careful follow-up and two surgery) died, and one careful follow-up patient withdrew consent before the 6-month follow-up visit. There were few missed visits: none (0%) of the 99 surgery patients and one (1%) of the 98 careful follow-up patients missed the 6-month visit (Table 2). Of the 237 patients for whom baseline data had been received, the baseline visual acuity measurements were incomplete for four patients, one in the surgery group and three in the careful follow-up group. The numbers of patients with data submitted and entered at the time of the DSMC meeting are provided in Table 2.

Visual Acuity

At 6 months, 42.7% (38/89) of patients in the careful follow-up group had improved three or more lines of vision, and an additional 44.9% (40/89) of the patients had little or no change (Table 4). In the surgery group, the corresponding values were 32.6% (30/92) and 43.5% (40/92), respectively.

Unadjusted RRs for three or more lines better and three or more lines worse for the 3-, 6-, and 12-month follow-up visits for all patients in the trial are presented in Table 4. There were no significant differences between surgery and careful follow-up at 3, 6, and 12 months of follow-up for getting better, although the trend favored careful follow-up (eg, unadjusted RR at 6 months, 0.76; 95% CI, 0.52 to 1.12). There was a significantly greater risk of getting worse from surgery compared with careful follow-up at 3, 6, and 12 months (unadjusted RR at 6 months, 1.94; 95% CI, 1.02 to 3.69; P=.04). There was no significant difference between groups in the proportion of patients whose vision was better than 20/200 in the study eye at randomization but whose vision was 20/200 or worse in the study eye at 6 months of follow-up (19% in the careful follow-up group vs 31% in the surgery group; P=.22).

There were no significant differences between the treatment groups among patients whose change in visual acuity at 6 months went from "off the chart" (count fingers or worse) to "on the chart" (better than count fingers)—45% in the surgery group vs 39% in the careful follow-up group—or from on the chart to off—8% in the surgery group vs 4% in the careful follow-up group.

When analyses were stratified on the prespecified variables (Table 5), the adjusted results were consistent with unadjusted comparisons except that significantly (P=.03) greater beneficial effects of careful follow-up occurred in persons aged 65 years or older. For this reason adjusted RRs for getting better are not given for age, and the RRs are shown separately for the two age groups.

In the logistic regression analysis examining the 6-month follow-up data, no significant interactions with treatment were observed, and only diabetes met the criteria for confounding. The adjusted OR estimates (Table 6) were 0.74 (95% CI, 0.39 to 1.38; P=.34) for getting better and 1.96 (95% CI, 0.87 to 4.41; P=.10) for getting worse (unadjusted

ORs of 0.65 [95% CI, 0.35 to 1.19] and 2.23 [95% CI, 1.02 to 4.87], respectively). Although the results are not statistically significant, the ORs of 0.74 and 1.96 suggest that surgery provides less improvement than does careful follow-up and may be more hazardous.

None of the analyses detected any indication of an interaction of treatment effect with progressive status (defined in three separate ways). There was no apparent beneficial effect of surgical experience; the trend favored less experienced surgeons, regardless of which definition of experience was used.

Visual Fields

There was no beneficial effect of surgery compared with careful follow-up in terms of change in mean deviation of visual field at 3, 6, or 12 months. Treatment effects (change in mean deviation in the surgery group minus change in mean deviation in the careful follow-up group), adjusted using multiple linear regression for mean deviation at randomization, were −1.00 (SE=0.93; P=.29), −0.18 (SE=1.01; P=.86), and −0.56 (SE=1.17; P=.63) at 3, 6, and 12 months, respectively. A negative treatment effect indicates that there is a smaller improvement in mean deviation in the surgery group than in the careful follow-up group. When we adjusted for each of the other variables (noted in the "Methods" section) along with mean deviation at randomization, we found no interactions with treatment group, and the adjusted treatment effect was never statistically significant.

Adverse Events

Patients who received surgery experienced both intraoperative and postoperative adverse events. One patient developed central retinal artery occlusion during surgery and had only light perception vision at 6 months. The same proportion of patients whose surgery lasted longer than 120 minutes as those whose surgery lasted 30 to 120 minutes experienced a loss of three or more lines of vision. Two surgical patients experienced an immediate loss of light perception following surgery and had loss of vision that persisted to the 12-month visit. Two careful follow-up patients had no light perception at the 6-month follow-up visit, and one of these had improved to light perception at 12 months. Pain was the most common adverse event in the surgery group (17% at 1 week compared with 3% in the careful follow-up group). Diplopia was the next most common complication (8% in the surgery group compared with 1% in the careful follow-up group at 1 week); by 3 months, there was no difference in diplopia between the two groups. No differences were observed between the two groups in medical complications during the 12-month follow-up period.

Table 3.—Characteristics of Participants at Randomization, by Treatment Group*

Patient Characteristics		Treatment Group: Careful Follow-up, No. (%) (n=122)	Treatment Group: Surgery, No. (%) (n=115)	P
Age, y				
50-59		19 (15.6)	17 (14.8)	
60-69		49 (40.2)	53 (46.1)	
70-79		42 (34.4)	34 (29.6)	.68
80-89		12 (9.8)	11 (9.6)	
≥90		0	0	
Sex				
Male		70 (57.3)	65 (56.5)	.89
Female		52 (42.6)	50 (43.5)	
Race				
White		113 (92.6)	113 (98.3)	
Black		3 (2.5)	0	
Hispanic		6 (4.9)	2 (1.7)	.09
Asian		0	0	
Other		0	0	
Enrollment type				
Regular entry		108 (88.5)	89 (77.4)	.02
Late entry		14 (11.5)	26 (22.6)	
Days between onset and randomization				
0 to 1		0	0	
2 to 4		15 (12.4)	15 (13.0)	
5 to 7		29 (24.0)	17 (14.8)	.27
8 to 14		67 (55.4)	69 (60.0)	
≥15		10 (8.3)	14 (12.2)	
Unknown		1	0	
Hypertension				
Yes		63 (52.1)	54 (47.0)	
No		58 (47.5)	61 (53.0)	.43
Unknown		1	0	
Diabetes				
Yes		39 (32.2)	21 (18.3)	
No		82 (67.8)	94 (81.7)	.01
Unknown		1	0	
Visual acuity at randomization†				
Snellen equivalent	Log MAR			
20/64 to >20/100	0.50 to <0.70	23 (19.3)	28 (24.6)	
20/100 to >20/200	0.70 to <1.00	16 (13.5)	26 (22.8)	
20/200 to >20/800	1.00 to <1.60	42 (35.3)	27 (23.7)	.17
20/800 to >CF	1.60 to <2.00	13 (10.9)	10 (8.8)	
CF to no light perception	≥2.0 (off chart)	25 (21.0)	23 (20.2)	
Unknown		3	1	
Mean deviation at randomization‡				
>−3 dB		1 (1.0)	1 (1.0)	
−3 to −5.99 dB		3 (2.8)	9 (9.0)	
<−5.99 to −20 dB		35 (33.0)	32 (32.0)	.21
<−20 dB		67 (63.2)	58 (58.0)	
Unknown		16	15	

*Data as of September 8, 1994.
†Log MAR indicates log of the minimum angle of resolution; CF, able to count fingers; and greater than symbol (>), better than.
‡Humphrey Visual Field using StatPac 24-2. Mean deviation is a weighted average of a patient's visual field deviations (in decibels [dB]) from a standard set of normal age-specific values.

COMMENT

Optic nerve decompression surgery, as evaluated in the IONDT, appears to be of no value to most patients with NAION and may lead to further visual deterioration. An unexpectedly high rate of spontaneous improvement in visual acuity (42.7%) was observed at 6 months in the careful follow-up group.

Optic nerve decompression surgery did not result in improved visual acuity compared with careful follow-up in patients with NAION and was associated with a lower rate of improvement. At 3, 6, and 12 months of follow-up, patients receiving surgery had a greater risk of losing three or more lines of vision. There

Table 4.—Association Between Follow-up Visual Acuity and Treatment Group, All Participants*

	No. of Patients	Follow-up Visual Acuity			RR (95% CI)†	
		≥3 Lines Better, %	Little Change, %	≥3 Lines Worse, %	≥3 Lines Better	≥3 Lines Worse
3 months						
Careful follow-up	109	39.5	53.2	7.3	0.69 (0.47-1.02) P=.06	2.51 (1.19-5.30) P=.02
Surgery	103	27.2	54.4	18.5		
6 months						
Careful follow-up	89	42.7	44.9	12.4	0.76 (0.52-1.12) P=.16	1.94 (1.02-3.69) P=.04
Surgery	92	32.6	43.5	23.9		
12 months						
Careful follow-up	51	41.2	51.0	7.8	0.71 (0.42-1.22) P=.22	3.25 (1.23-8.58) P=.02
Surgery	51	29.4	45.1	25.5		

*Data as of September 8, 1994.
†RR indicates relative risk; and CI, confidence interval. Relative risk of getting better=percentage of total surgery patients getting better divided by percentage of total careful follow-up patients getting better. Relative risk of getting worse=percentage of total surgery patients getting worse divided by percentage of total careful follow-up patients getting worse.

Table 5.—Association Between Visual Acuity and Treatment Group at 6-Month Follow-up, by Subgroup*

Subgroups	No. of Patients	Follow-up Visual Acuity			Adjusted RR (95% CI)†	
		≥3 Lines Better, %	Little Change, %	≥3 Lines Worse, %	≥3 Lines Better	≥3 Lines Worse
Age, y‡						
<65						
Careful follow-up	35	40.0	48.6	11.4	1.21 (0.70-2.09)‡ P=.49	1.91 (1.00-3.66) P=.05
Surgery	31	48.4	32.2	19.4		
≥65						
Careful follow-up	54	44.4	42.6	13.0	0.55 (0.33-0.94)‡ P=.03	
Surgery	61	24.6	49.2	26.2		
Sex						
Male						
Careful follow-up	52	34.6	48.1	17.3	0.76 (0.52-1.10) P=.14	2.00 (1.04-3.80) P=.04
Surgery	49	32.7	40.8	26.5		
Female						
Careful follow-up	37	54.1	40.5	5.4		
Surgery	43	32.6	46.5	20.9		
Enrollment status						
Regular entry						
Careful follow-up	77	44.2	44.1	11.7	0.79 (0.54-1.15) P=.21	1.96 (1.04-3.71) P=.04
Surgery	71	35.2	38.0	26.8		
Late entry ("progressive")						
Careful follow-up	12	33.3	50.0	16.7		
Surgery	21	23.8	61.9	14.3		
Hypertension						
Yes						
Careful follow-up	45	53.3	35.6	11.1	0.77 (0.53-1.11) P=.16	1.93 (1.00-3.75) P=.04
Surgery	46	37.0	43.4	19.6		
No						
Careful follow-up	44	31.8	54.6	13.6		
Surgery	46	28.3	43.4	28.3		
Diabetes						
Yes						
Careful follow-up	31	54.8	35.5	9.7	0.81 (0.55-1.19) P=.28	1.80 (0.93-3.48) P=.08
Surgery	18	38.9	50.0	11.1		
No						
Careful follow-up	58	36.2	50.0	13.8		
Surgery	74	31.1	41.9	27.0		
Visual acuity at randomization§						
Log MAR <2 (on chart)						
Careful follow-up	71	42.3	43.6	14.1	0.76 (0.52-1.11) P=.15	1.95 (1.02-3.71) P=.04
Surgery	72	27.8	47.2	25.0		
Log MAR ≥2 (off chart)						
Careful follow-up	18	44.4	50.0	5.6		
Surgery	20	50.0	30.0	20.0		

*Data as of September 8, 1994.
†RR indicates relative risk; and CI, confidence interval. Adjusted for subgroup using Mantel-Haenszel method.
‡Relative risk for getting better computed separately for each age group instead of adjusted because there was significant interaction between treatment and age.
§Log MAR indicates log of the minimum angle of resolution.

Table 6.—Association Between Visual Acuity and Treatment Group at 6-Month Follow-up Adjusted Using Multiple Logistic Regression Analysis

Logistic Regression Model	Odds Ratio (95% Confidence Interval)	
	≥3 Lines Better	≥3 Lines Worse
Treatment group only, surgery vs careful follow-up	0.65 (0.35-1.19)	2.23 (1.02-4.87)
Multivariable		
Surgery vs careful follow-up	0.74 (0.39-1.38)	1.96 (0.87-4.41)
Diabetes, yes vs no	1.83 (0.91-3.68)	0.44 (0.16-1.25)
Visual acuity at randomization worse by ≥3 lines*	1.16 (1.00-1.34)	0.83 (0.67-1.02)

*Visual acuity is a continuous variable.

was no apparent benefit to IONDT patients operated on by more experienced surgeons, regardless of how we defined experience. Our findings of no benefit and possible greater visual loss in the surgery group were consistent across subgroups. Adjusted results using prespecified variables were consistent with unadjusted comparisons. We did not detect any meaningful differences between groups in medical complications during the 12-month follow-up period, but the relatively small size of our study population may have precluded detection of such differences.

We believe that our failure to observe a statistically significant difference between treatment groups is because surgery is of no benefit, not because our sample size is too small. Although it is impossible to have a statistically significant result supporting any null hypothesis (of no treatment effect), narrow CIs around the estimate of an RR or OR, that include 1.0, increase our belief in the validity of this result. As part of the decision to cease recruitment to the IONDT, the DSMC considered whether continuing enrollment would increase the power of the study to detect a possible true beneficial effect of surgery. Assuming we had continued to enroll and follow-up 135 patients in each arm, as was originally planned, and 42.7% of patients in the careful follow-up group had improved vision at 6 months (Table 4), then even if 100% (all 43) of the surgery patients yet to be followed up at 6 months showed improvement of three or more lines of vision, the unadjusted RR for improved vision would be 1.26 (95% CI, 0.98 to 1.61; P=.07). This corresponds to an overall improvement in the surgery group of 54%, in contrast with the 32.6% we have observed. In addition, our evidence indicates that surgery may be harmful.

We were unable to demonstrate any benefit of surgery in IONDT patients defined as having progressive visual loss. Although our analyses are based on relatively small numbers of patients, regardless of how we define progressive (12 careful follow-up patients and 21 surgery patients in the late-entry group; 11 careful follow-up patients and 16 surgery patients in the late-entry subgroup who worsened three or more lines before randomization; and 54 careful follow-up patients and 45 surgery patients who perceived a worsening of vision before randomization), the consistency of our findings across operational definitions of progression increases our confidence in this conclusion. We recognize that our definitions of progressive status may be limited yet have been unable to identify preferable definitions.

Our most encouraging finding was the high percentage of patients in the careful follow-up group who had visual acuity improvement. A total of 42.7% of patients in this group improved by three or more lines over baseline evaluation within 6 months. This improvement is greater than indicated in the literature before 1989,[7,8] when favorable results from ONDS were first reported. With one exception,[17] spontaneous improvement in NAION was reported to be less than 10%, independent of how improvement was defined. Subsequent case series published since 1989,[18-20] have reported higher rates of improvement, some as high as 33%. One reason for the high rate of improvement that we observed may be that we excluded patients with vision better than 20/64, whereas other studies did not; some patients in other studies may have had such good vision at baseline that it was not possible for them to improve their visual acuity by two or more lines. Another possible reason is that prior studies may have excluded patients from the analyses, thereby affecting the estimate of proportion improved. Finally, follow-up times in prior studies varied and may have been insufficient in some cases to observe improvement.

The observed improvement in the careful follow-up group and the potential harm to vision from surgery evident in the IONDT lead us to recommend that ONDS be abandoned for patients with NAION. Although we are encouraged by the high proportion of patients who experience some spontaneous improvement, NAION remains a condition that has an unknown etiology and no known means of effective prevention or treatment. Future research must focus on increasing our understanding of factors leading to development of NAION and factors associated with prognosis. By achieving a better understanding of the pathophysiology and natural history of the disease, effective prevention and treatment strategies may be developed.

The Ischemic Optic Neuropathy Decompression Trial was supported by grants from the National Eye Institute (EY09608, EY09545, EY09556, EY09555, EY09554, EY09576, EY09565, EY09551, EY09599, EY09584, EY09578, EY09572, EY09575, EY09567, EY09598, EY09550, EY09553, EY09566, EY09569, EY09579, EY09571, EY09568, EY09557, EY09552, EY09570, EY09582, and EY09626).

The participants in the Ischemic Optic Neuropathy Decompression Trial Research Group as of November 1994 were as follows:

Writing Committee: Kay Dickersin, PhD; Donald Everett, MA; Steven Feldon, MD; Frank Hooper, ScD; David Kaufman, DO; Shalom Kelman, MD; Patricia Langenberg, PhD; Nancy J. Newman, MD; P. David Wilson, PhD; and Z. Suzanne Zam.

Clinical Centers: *Allegheny General Hospital, Pittsburgh, Pa*: John Kennerdell, MD (principal investigator); Anna Tyutyunikov, MD (coordinator); Russell Edwards, MD (1992-1993); Todd Goodglick, MD (1992-1993); Deborah Lang; and Kimberly Peele, MD. *Anheuser-Busch Eye Institute, St Louis (Mo) University Health Sciences Center*: Sophia Chung, MD (principal investigator); Diana Mekelburg, COT (coordinator); John Holds, MD; and John Selhorst, MD. *Carolinas Medical Center, Charlotte, NC*: Mark Malton, MD (principal investigator); Sonia Armstrong, COT (coordinator, 1992-1993); Yvonne McCracken, MPH (coordinator); Eugene Benjamin, MD; Carol Dellinger (1992-1993); Traci Hunter Medlin, COT (1992-1993); Barbara Kinsler; Mike McOwen, CLP; Donna Russell, COT (1992-1994); and Timothy Saunders, MD. *Cleveland (Ohio) Clinic Foundation*: Gregory Kosmorsky, DO (principal investigator); Tina Kiss (coordinator); Cate Reinhard (coordinator); Laura DeVenne; Janet Edgerton; Tami Fecko; Susannah Hanson; Brian Kraus; Deborah Ross; Nancy Tomsak; Pamela Vargo; and Rufus Willis. *Doheny Eye Institute, Los Angeles, Calif*: Steven Feldon, MD (principal investigator); Kerry Zimmerman, MS (coordinator); Kristin Anderson, COMT (1992-1994); Richard Cortez (1992-1994); Karen DeBlanc, COA (1992-1993); Judy Hulse, COT (1993- 1994); Ronald B. Morales (1992-1993); Tracy Nichols, CRA; Lillian Reyes, COT (1992-1994); Nadine Rodarte-Ochoa, COT; Daniel Romo; Alfredo Sadun, MD; Mary Steber, COMT (1994); and Frances Walonker, COMT (1994). *Emory University, Atlanta, Ga*: Nancy J. Newman, MD (principal investigator); Donna Loupe, BA (coordinator); Diana Coffman, MMSc (coordinator, 1992-1994); Harvey Cole III, MD; and Ted Wojno, MD. *Henry Ford Hospital, Detroit, Mich*: Barry Skarf, MD (principal investigator); Colleen Wojtala (coordinator); Mark Croswell; Wendy Gilroy; Christian Mageli; Dena McDonald; and George Ponka. *University of Texas, Houston*: Rosa Tang, MD (principal investigator); Melissa Hamlin (coordinator); Jewel Curtis; Jay Forman; Kenneth Hyde, MD; Kirk Mack; and Portia Tello. *Jules Stein Eye Institute, Los Angeles, Calif*: Anthony Arnold, MD (principal investigator); Bernice Cibener, BA (coordinator); Melody Acero; Bobbi Ballenberg, COMT; Anne Bolton; Robert Goldberg, MD; Lynn Gordon, MD; Michael Heneghan; Howard Krauss, MD; Jackie Sanguinet; Robert Stalling; and Jenja Yadegaran, BS. *W. K. Kellogg Eye Center, University of Michigan, Ann Arbor*: Wayne Cornblath, MD (principal investigator); Barbara Michael (coordinator); Donna Campbell, COT; Cheryl Caudill, COT (1992-1994); Christine Nelson, MD; and Jonathan

Trobe, MD. *Mason Institute of Ophthalmology, Columbia, Mo*: Lenworth N. Johnson, MD (principal investigator); Gaye Baker (coordinator); Coy Cobb, CRA, COT; Philip Custer, MD; Sharon Turner, COA; and Roy Wilson, MS, COMT (1992-1993). *Mayo Clinic, Rochester, Minn*: Brian Younge, MD (principal investigator); Jacqueline Leavitt, MD (co-principal investigator); Rebecca Nielsen, LPN (coordinator); Jody Allen (1992-1994); Barbara Eickhoff, COT; James Garrity, MD; Jacqueline Ladsten; Kathleen LeBarron, COA; Thomas P. Link, BA; Jay Rostvold; and Karen Weber. *Medical College of Virginia, Richmond*: Warren Felton III, MD (principal investigator); Tracy Boney, AS (coordinator); Danielle Gabriel, BS (coordinator, 1992-1994); Daniel David, MS; Lahn Fendelander, MS; Daniel Geller, MD; Timothy Jordan, MD; Christian Kim, MD; Craig Munger, MD; Jo Anne Romandy, COA; George Sanborn, MD; Bradley Schwartz, MD; Carl Sheusi, BA (1993-1994); Constance Smith, MD; Kathy Talley, AS; and Sandya Thimmappa, BS (1993). *Michigan State University, East Lansing*: David Kaufman, DO (principal investigator); Eric Eggenberger, DO (co-principal investigator); Suzanne Bickert, RN (coordinator); Robert Granadier, MD; Sandra Holliday; Thomas Moore, MD; and Jaya Varadarajan, MD. *State University of New York, Syracuse*: Deborah Friedman, MD (principal investigator); Patricia Jones, LPN, COT (coordinator); Haris Amin, MD; Thomas Bersani, MD; Cynthia Briglin, MD; James Fooks; Michael Graham, MD; Milton James, MD; Gary Michalec (1992-1994); and Hoang Nguyen (1992). *University of California, San Francisco*: Jonathan Horton, MD (principal investigator); Maeve Chang, BA (coordinator); Lou Anne Aber, COA; Erik Lindstrom, COMT; and Stuart Seiff, MD. *University of Florida, Gainesville*: John Guy, MD (principal investigator); Z. Suzanne Zam, BS (coordinator); Amye Francis, CO; Latif Hamed, MD; Alan Lessner, MD; Donna McDavid, COMT; and Diana Shamis, MHSE. *University of Illinois, Chicago*: James Goodwin, MD (principal investigtor); Martin E. Lindeman, COMT (coordinator); Allen Putterman, MD; and Phyllis Bobak, PhD. *University of Kentucky, Lexington*: Robert Baker, MD (principal investigator); Judy Beck (coordinator); David Cowen, MD; Avrom Epstein, MD (1992-1994); Michael Hanson; and Toni Scoggins, COA. *University of Maryland, Baltimore*: Shalom Kelman, MD (principal investigator); Ann M. Rodavitch, MA (coordinator); Brenda Gore (coordinator, 1992-1993); Andrea Blake, MA (coordinator, 1993-1994); Michele Heroux, CRA; Rani Kalsi; Charlene Krauch, COMT; and Mary Ann Millar, COMT. *University of South Carolina, Columbia*: Mitchell Wolin, MD (principal investigator); Rita Jean Brady, COA (coordinator, 1992-1994); Regina Hansen, COA (coordinator); Michael Briggs (1992-1993); Karkarla V. Chalam, MD; Barbara Danner; Beverly Simons, COT; and Anne Stewart, CO. *University of Utah, Salt Lake City*: Kathleen Digre, MD (principal investigator); Lizbeth Malmquist-Webb (coordinator); Terrell Blackburn (coordinator, 1992-1993, deceased); Susan Baggaley (coordinator, 1993-1994); Richard Anderson, MD; Charles Juarez; Bonnie Kaye; Paul Langer, MD; Aditya Mishra, MD (1993-1994); Paula Morris; Sandra Osborn; Bhupendra Patel, MD; Tessie Priskos; Sandra Staker; and Judith Warner, MD. *University of Virginia, Charlottesville*: Steven Newman, MD (principal investigator); Christine Evans, COT (coordinator); Allison Aylor, COT; Carolyn Childress, COA; Helen Dickerson, RN; Jane Fleming, BA; Nomine Harris, BA; L. Sharon Hoyle, COMT (1992-1994); Ellen Murphy, COT (1992-1994); James Scott, RBP; Karen Summerville, COMT; Mariann Terrell, CO; and Lillian Tyler, COA. *West Virginia University, Morgantown*: John Linberg, MD (principal investigator); Lenore Breen, MD (principal investigator, 1992-1993); Michelle Michael, COT (coordinator); Charlene Campbell, COT; Brian Ellis, MD; Nancy Groves, COA; Robert Hobson (1992-1993); Gordon McGregor (1993-1994); and Laura Shepherd, COA. *William Beaumont Hospital, Royal Oak, Mich*: Edward Cohn, MD (principal investigator); Patricia Manatrey (coordinator); Sara Casey; Robert Granadier, MD; John Johnson; Coletti Kronner; Virginia Regan; and Patricia Streasick.

Resource Centers: *Chairman's Office, University of Maryland School of Medicine, Baltimore*: Shalom Kelman, MD (study chairman); Michael Elman, MD (vice chairman, 1992-1994); Andrea Blake, MA (1993-1994); and Ann M. Rodavitch, MA (administrator). *Coordinating Center, University of Maryland School of Medicine, Baltimore*: Kay Dickersin, PhD (director); Frank Hooper, ScD (associate director); Roberta Scherer, PhD (project coordinator); Barbara Crawley, MS; Michael Elman, MD (1992-1994); Cheryl Hiner; Lucy Howard; Patricia Langenberg, PhD; Olga Lurye; Robert McCarter, ScD; Sara Riedel; Michelle Sotos; Laureen Spioch; Joann Starr (1992-1994) Judy Urban (1993-1994); Mark Waring; and P. David Wilson, PhD. *National Eye Institute, Bethesda, Md*: Donald Everett, MA.

Committees: *Data Analysis Committee*: Barbara Crawley, MS; Kay Dickersin, PhD; Frank Hooper, ScD; Patricia Langenberg, PhD; Robert McCarter, ScD; Roberta Scherer, PhD; and P. David Wilson, PhD. *Executive Committee*: Shalom Kelman, MD (chair); Kay Dickersin, PhD; Michael Elman, MD (1992-1994); Donald Everett, MA; and Frank Hooper, ScD. *Quality Assurance Committee*: Frank Hooper, ScD (chair); Shalom Kelman, MD; Roberta Scherer, PhD; Danielle Gabriel (1992-1994). *Steering Committee*: Shalom Kelman, MD (chair); Kay Dickersin, PhD; Michael Elman, MD (1992-1994); Donald Everett, MA; Steven Feldon, MD; Frank Hooper, ScD; David Kaufman, DO; Nancy J. Newman, MD; and Z. Suzanne Zam, BS. *Surgical Quality Assurance Committee*: Steven Feldon, MD (chair); Robert Baker, MD; Frank Hooper, ScD; Shalom Kelman, MD; Gregory Kosmorsky, DO; and Stuart R. Seiff, MD.

The IONDT Research Group would like to acknowledge the members of the *Data Safety and Monitoring Committee*: Marian Fisher, PhD (chair); Phil Aitken, MD; Roy Beck, MD; Andrea LaCroix, PhD; Simmons Lessell, MD; Rev Kenneth MacLean; Kay Dickersin, PhD (ex officio); Michael Elman, MD (ex officio, 1992-1994); Donald Everett, MA (ex officio); and Shalom Kelman, MD (ex officio).

References

1. Hayreh SS. *Anterior Ischemic Optic Neuropathy*. New York, NY: Springer Verlag NY Inc; 1975.
2. Hayreh SS. Anterior ischemic optic neuropathy. *Arch Neurol.* 1981;38:675-678.
3. Hayreh SS. Anterior ischemic optic neuropathy: differentiation of arteritic from non-arteritic type and its management. *Eye.* 1990;4:25-41.
4. Johnson LN, Arnold AC. Incidence of non-arteritic anterior ischemic optic neuropathy: population based study in the state of Missouri and Los Angeles County, California. *J Neuroophthalmol.* 1994;14:38-44.
5. Ischemic Optic Neuropathy Decompression Trial (IONDT) Research Group. *Manual of Operations*. Baltimore: University of Maryland at Baltimore; 1992;chap 1:1-2.
6. Beri M, Klugman MR, Kohler JA, Hayreh SS. Anterior ischemic optic neuropathy, VII: incidence of bilaterality and various influencing factors. *Ophthalmology.* 1987;94:1020-1028.
7. Boghen DR, Glaser JS. Ischemic optic neuropathy: a clinical profile and natural history. *Brain.* 1975;98:689-708.
8. Repka MX, Savino PJ, Schatz NJ, Sergott RC. Clinical profile and long-term implications of anterior ischemic optic neuropathy. *Am J Ophthalmol.* 1983;96:478-483.
9. Sergott RC, Cohen MS, Bosley TM, Savino PJ. Optic nerve decompression may improve the progressive form of nonarteritic ischemic optic neuropathy. *Arch Ophthalmol.* 1989;107:1743-1754.
10. Kelman SE, Elman MJ. Optic nerve sheath decompression for non-arteritic ischemic optic neuropathy improves multiple visual function parameters. *Arch Ophthalmol.* 1991;109:667-671.
11. Spoor TC, Wilkinson MJ, Ramocki JM. Optic nerve sheath decompression for the treatment of progressive nonarteritic ischemic optic neuropathy. *Am J Ophthalmol.* 1991;111:724-728.
12. Spoor TC, McHenry JG, Lau-Sickon L. Progressive and static nonarteritic ischemic optic neuropathy treated by optic nerve sheath decompression. *Ophthalmology.* 1993;100:306-311.
13. Westheimer G. Scaling of visual acuity measurements. *Arch Ophthalmol.* 1979;97:327-330.
14. Ederer F, Hiller R. Clinical trials, diabetic retinopathy, and photocoagulation. *Surv Ophthalmol.* 1975;19:267-286.
15. Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36). *Med Care.* 1992; 30:473-481.
16. Kleinbaum DG, Kupper LL, Morgenstern H. *Epidemiologic Research: Principles and Quantitative Methods.* New York, NY: Van Nostrand; 1982:296-301.
17. Ellenberger C Jr, Keltner JL, Burde RM. Acute optic neuropathy in older patients. *Arch Neurol.* 1973;28:182-185.
18. Yee RD, Selky AK, Purvin VA. Outcomes of optic nerve sheath decompression for nonarteritic ischemic optic neuropathy. *J Neuroophthalmol.* 1994;14:70-76.
19. Arnold AC, Hepler RS. Natural history of nonarteritic anterior ischemic optic neuropathy. *J Neuroophthalmol.* 1994;14:66-69.
20. Rizzo JF, Lessell S. Optic neuritis and ischemic optic neuropathy. *Arch Ophthalmol.* 1991;109:1665-1672.