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Comparison of Visual Outcomes of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients with and without Diabetes Mellitus

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Purpose: Diabetic patients have a greater risk of nonarteritic anterior ischemic optic neuropathy (NAION) than nondiabetic patients. We compare visual outcomes, prevalence of bilateral/sequential ION, and predictors of visual outcomes in NAION between diabetic and nondiabetic patients.

Design: Case-control study.

Participants: All 231 patients with NAION seen by the Neuro-Ophthalmology Service, Wilmer Eye Institute, between 2002 and 2011 were screened for study inclusion.

Methods: Patients presenting within 4 weeks of symptom onset (30 with diabetes mellitus, 62 control patients) were included in baseline demographic assessments of vascular risk factors. Interval and final visual outcomes (logarithm of the minimum angle of resolution [logMAR] visual acuity [VA]) were evaluated in the 81 patients in this group with clinical follow-up for $\geq$3 months, and population average logistic regression models were used to determine risk factors for worse visual outcomes.

Main Outcome Measures: Visual acuity at last follow-up.

Results: The median follow-up duration was 38.7 weeks in diabetic patients and 52.9 weeks in nondiabetic patients. The majority (92.5%) of patients presented within 2 weeks of symptom onset. In nondiabetic patients, the most prevalent risk factor for NAION was hyperlipidemia (62.9%); for diabetic patients, NAION risk factors included hypertension (83.3%), hyperlipidemia (83.3%), and small cup-to-disc ratio (63.3%). Sequential NAION occurred in 36.8% of diabetic patients and 20.9% of nondiabetic patients. At last follow-up, 48% of diabetic and 62% of nondiabetic patients had VA better than 20/40. Similar proportions of diabetic and nondiabetic patients (8 [27%] diabetic and 14 [22.5%] nondiabetic patients) recorded a final follow-up vision of 1.0 logMAR or worse at a minimum of 3 months. Ischemic heart disease (odds ratio [OR], 7.21; $P < 0.001$) and greater age (OR, 1.05; $P = 0.045$) were associated with increased risk for final VA <20/200 in the multiple regression model (OR, 4.35; $P = 0.011$).

Conclusions: The VA at presentation and at final follow-up in diabetic patients with NAION were not significantly different from nondiabetic controls, although diabetic patients had a higher prevalence of cardiovascular risk factors. Ischemic heart disease and greater age, but not diabetes, independently correlated with worse VA outcome. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology*

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute-onset optic neuropathy in persons older than 50 years of age, with an incidence of 2.3 to 10.2 per 100 000 in the general population.[1,2] The incidence is higher in patients with increased risk of atherosclerotic disease,[3] and although the primary risk factor has been suggested to be an anatomically crowded "disk at risk" with a small optic nerve head diameter and cup-to-disc (C/D) ratio,[4] its presence is not required to make the diagnosis. Nonarteritic anterior ischemic optic neuropathy typically occurs in patients older than 50 years of age, but the incidence in younger patients is on the rise, perhaps because of increased prevalence of atherosclerotic risk factors. It may have an incidence as high as 82 per 100 000 in diabetic patients aged $\geq$65 years.[5,6] The disorder is thought to have a vascular cause with hypoperfusion and vascular dysregulation of the posterior ciliary arteries leading to axonal ischemia and swelling, followed by retinal ganglion cell death.[7] In addition, the axonal edema itself may cause a secondary compartment syndrome at the level of the lamina cribrosa and exacerbate retinal ganglion cell loss.

Although diabetic patients have a greater risk of NAION,[6,8] it is unknown whether their visual outcomes are different from nondiabetic patients with NAION. Existing data on visual outcomes in those with NAION and diabetes who were enrolled in the Ischemic Optic Neuropathy Decompression Trial indicate that diabetes was a potential

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confounder, with a trend toward better visual outcomes in diabetic subjects; however, despite randomization, a greater number of diabetic subjects were assigned to the "careful follow-up" group, which as a whole had a better outcome than the surgical group.[9] The prevalence of diabetes has increased in the general population since the Ischemic Optic Neuropathy Decompression Trial was published, and treatment has changed as well, with better glycemic control often being present. In addition, some medications used to treat diabetes, such as sulfonylureas, have been reported to have a neuroprotective effect in animal models.[10] Therefore, we sought to evaluate the visual outcomes of diabetic patients with NAION compared with age- and gender-matched nondiabetic NAION controls.

Methods

We conducted a retrospective chart review of all patients seen in the Neuro-Ophthalmology Division of the Wilmer Eye Institute from 2002 to 2011 with a clinical diagnosis of NAION made by one of the senior authors (N.R.M., P.S.S.) on the basis of the presence of hyperemic optic disc swelling associated with acute, painless loss of vision acuity or visual field and no evidence for an alternative diagnosis. This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board and was conducted in accord with Health Insurance Portability and Accountability Act regulations. Inclusion was restricted to patients who had presented within 4 weeks of symptoms to verify diagnostic criteria and with a minimum of 6 weeks of follow-up.

Of 231 patients with NAION or suspected NAION, 128 did not meet follow-up criteria or did not present within 4 weeks of symptoms and study of 11 other records revealed a subsequent diagnosis other than NAION. Thus, 92 patients were included in this study.

We classified 30 patients as diabetic by chart review, based on patient self-report, available laboratory testing results showing abnormal fasting blood glucose or elevated glycosylated hemoglobin levels, and reports from the patient's primary care physician or endocrinologist. Five of these patients had "borderline diabetes" and were not taking glycemic medications; however, they were classified as diabetic for the purposes of this study because of the high risk of conversion to diabetes. The remaining 62 patients were found to be nondiabetic. The 2 groups, diabetic and nondiabetic, were compared with respect to demographic data, risk factors for NAION (C/D ratio <0.3, obstructive sleep apnea, ischemic heart disease, hypertension, hyperlipidemia), and visual outcomes. These factors were examined at the initial visit, at initial follow-up 4–6 weeks later, and at the final follow-up visit. Visual acuity (VA) was converted from Snellen to logarithm of the minimum angle of resolution (logMAR) units to aid in analysis.

Color vision was recorded as X of 10 Hardy-Rand-Rittler plates. If no color plates were seen, then gross color identification was assessed and converted to a color plate equivalent of 0.08/10 (1 color identified), 0.17/10 (2 colors identified), or 0.25/10 for 3 or more colors identified.

Statistical Methods

To compare the visual and demographic characteristics between diabetic and nondiabetic patients and between VA better or worse than 20/200 (1.0 logMAR) at presentation, chi-square tests were used for categoric variables, including gender, patient health history, and categorized VA at presentation and at the last recorded visit. Student t test was used for age, and the nonparametric Kruskal–Wallis test was used for the change in VA from presentation to the last recorded visit because of its skewed distribution. Generalized estimating equation population-averaged logistic regression models were used to examine the comorbidities associated with a final VA of worse than 1.0 logMAR in affected eyes. The generalized estimating equation models were used to account for the correlation among the repeated measures for the same patients. A P value ≤ 0.05 was treated as statistically significant. All the analyses were carried out in Stata 14.1 (StataCorp LP, College Station, TX).

Results

Patient demographics are shown in Table 1. Simultaneous NAION was seen in 1 patient in each group. Second eye involvement in those patients who presented with unilateral NAION was recorded in 11 (37.9%) diabetic patients and 13 (21.3%) of age/gender-matched nondiabetic controls, although it was a remote occurrence in most cases, because 1 diabetic patient and 4 controls had second eye involvement in the study follow-up period. The majority (92.5%) of patients were evaluated within 2 weeks of symptom onset. Eleven patients had less than 3 months of follow-up and were included in the baseline analyses but not the final visual outcomes. The remaining 81 patients (88.0%) had at least 3 months of follow-up, and 65 patients (70.7%) had follow-up data for ≥6 months. The median follow-up duration was 38.7 weeks in diabetic patients and 52.9 weeks in nondiabetic controls. Patients were not prescribed oral or intravenous corticosteroids as treatment for NAION. We did not identify a systematic reason for the difference in follow-up between the 2 groups in the neuro-ophthalmic clinic.

Risk Factors for Nonarteritic Anterior Ischemic Optic Neuropathy

We assessed the prevalence of reported risk factors for NAION in the 2 patient groups and found that ischemic heart disease was more prevalent in diabetic patients (Table 2), although overall

Table 1. Baseline Patient Characteristics

	Diabetic Patients	Nondiabetic Patients	All
No. of patients	30	62	92
% Female	36.7	35.5	35.9
% White	84.3	95	
Mean age/yrs (SD)	63.5 (5.9)	59.7 (11.2)	60.9 (9.9)
Age range (yrs)	51–73	37–85	37–85
Sequential NAION (%)	36.8	20.9	28.5
Bilateral NAION (%)	3.3	1.61	6.9
Second eye NAION during follow-up (%)	3.3	8.1	5.7
<2 wks from symptom onset to presentation (%)	90.0	95.2	92.5
Average number of wks follow-up (median)	110.2 (38.7)	136.4 (52.9)	123.3 (45.8)
No. patients with >6 mos follow-up (%)	23 (77)	42 (68)	65 (71)

NAION = nonarteritic anterior ischemic optic neuropathy; SD = standard deviation.