Visual Field Loss in Patients With Glaucoma Who Have Asymmetric Peripapillary Focal Arteriolar Narrowing

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Objective: To evaluate the relationship between peripapillary focal arteriolar narrowing and visual field defects.

Methods: From our institutional practice, we identified 31 patients with glaucoma who had peripapillary focal arteriolar narrowing in only one eye and compared visual field data between the two eyes. Mean deviation (MD) and corrected pattern standard deviation (CPSD) were recorded using Humphrey visual field testing at the time proximal narrowing was apparent on the fundus photograph. Visual field data from subsets of patients with mild and severe narrowing were also compared.

Results: The MD and CPSD were significantly worse in eyes with peripapillary focal arteriolar narrowing. The eyes with narrowing exhibited a mean MD of $-8.77 \pm 8.27$ dB and a mean CPSD of $3.01 \pm 3.42$ dB. Eyes without narrowing displayed a mean MD of $-4.52 \pm 6.64$ dB and a mean CPSD of $3.01 \pm 2.68$ dB ($P = .003$ for both). There was no significant difference in severity of the visual field defect between eyes with mild and severe arteriolar narrowing.

Conclusion: To our knowledge, this is the first study to show that the presence of peripapillary focal arteriolar narrowing is related to the severity of visual field loss in patients with glaucoma.

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In 1994, Rader et al described the focal narrowing of retinal vessels adjacent to the optic disc in eyes with glaucoma. They reported that these proximal constrictions were present in 42% of eyes with glaucoma but in only 5% that were normal. In glaucomatous eyes, the location of these arteriolar narrowings corresponded to the sector of the disc, with the greatest cupping in 91% of cases and to areas of absent retinal pigment epithelium in 87% of cases (β-peripapillary atrophy). Peripapillary focal arteriolar narrowing was not exclusive to eyes with glaucomatous optic nerve damage; 68% of eyes with nonarteritic anterior ischemic optic neuropathy also had proximal narrowing. Papastathopoulos and Jonas confirmed that this finding represents a true stenosis of the vessel lumen and is not an ophthalmoscopic artifact. Rankin and Drance noted that the location of the peripapillary narrowing correlated with the presence of a visual field defect in the corresponding superior or inferior hemi-field in 89% of cases. Moreover, in eyes with worse visual field loss in 1 hemi-field, Hall et al found narrower peripapillary vessels in the hemidisc corresponding to this defect. These findings indicate that peripapillary focal arteriolar narrowing may be related to the severity of glaucoma.

In this study, we evaluated the relationship between the presence of proximal narrowing and the severity of visual field defects. We selected patients who exhibited peripapillary focal arteriolar narrowing in only one eye and compared that eye’s visual field information with its fellow eye. We also hoped to determine whether the degree of narrowing correlated with exacerbation of the visual field defect.

METHODS

We examined the fundus photographs of 325 consecutive patients seen in a university-based glaucoma referral practice. All photographs were obtained from the medical records of patients at the Scheie Eye Institute in Philadelphia, Pa. For this review, written consent for the release of medical records was obtained from all patients. Photographs were examined for any evidence of focal arteriolar narrowing in the area spanning the peripheral optic disc rim and half the diameter of the
disc away from the rim. A focal narrowing was defined as an arterial segment that appeared narrower than the same artery immediately distal and proximal to the narrowing (Figure 1). The position of any focal narrowing was described using clock hours relative to the disc, and the degree of constriction was graded on a scale of 0 to 4. A score of 1 denoted mild narrowing, and 4 indicated very severe narrowing. The presence and grading of narrowings were agreed on by 2 investigators (V.B. and J.R.P.-S.).

We subsequently identified patients with primary open-angle glaucoma who had peripapillary focal arteriolar narrowing in only one eye. Visual field information including mean deviation (MD) and corrected pattern standard deviation (CPSD) was collected and compared between eyes with narrowing and their fellow eyes without narrowing. Data were recorded using visual field tests at the time focal narrowing was apparent on the fundus photograph. When focal constrictions were present in multiple photographs, we used visual field test results concurrent with the most recent photograph. In most cases, visual field tests were done on the same date that fundus photographs displayed proximal narrowing. In all cases, visual field tests were performed within 3 months of a fundus photograph showing arteriolar constriction. To investigate whether the degree of constriction affected the visual field defect, the data for eyes with focal constrictions graded 2 or worse (severe) were compared with data from those with constrictions graded 1 (mild). Statistical analysis was conducted using both paired and unpaired 2-tailed t tests.

| Table 1. Comparison of Mean Deviation and Corrected Pattern Standard Deviation in Eyes With and Without Peripapillary Focal Arteriolar Narrowing* |
|---------------------------------|-----------------|-----------------|-----------------|
|                                 | Eyes With Narrowing | Eyes Without Narrowing | P Value†        |
| Mean deviation, dB              | −8.77 ± 8.3      | −4.53 ± 6.6      | .003            |
| Corrected pattern standard deviation, dB | 5.01 ± 3.4      | 3.02 ± 2.7       | .003            |

*Data are presented as mean ± SD. †Determined using a paired 2-tailed t test.

Eighty-seven patients were identified who had primary open-angle glaucoma with good-quality photographs demonstrating peripapillary focal arteriolar narrowing. Of these 87 patients, 31 had focal narrowing in only one eye. Thirteen of these patients had constrictions graded 1, whereas the remaining 18 had constrictions graded 2 to 4. In all patients, arteriolar narrowing was static, or present in multiple photographs across time in the same location. Furthermore, the degree of stenosis either remained constant or grew worse in all cases (ie, we did not observe any reversibility in the arteriolar constrictions).

Eyes with proximal narrowing had significantly greater visual field defects than contralateral eyes without proximal narrowing (Table 1). The mean MD and CPSD were significantly worse in eyes with narrowing than in eyes without narrowing (mean difference in MD, 4.26; P = .003; mean difference in CPSD, 1.99; P = .003). Box plots for MD and CPSD illustrating the data spread are shown in Figure 2 and Figure 3.

To determine whether the degree of arteriolar constriction influences severity of the visual field defect, we compared the subsets of patients with constrictions graded 1 (mild) and those with constrictions graded 2 to 4 (more severe). No significant differences in MD or CPSD were noted between eyes with mild and severe narrowing (Table 2). In addition, no significant difference between mild and more severe constrictions was detected when evaluating MD and CPSD in eyes with narrowing and their fellow eyes without narrowing (Table 3).

Between the groups of eyes with and without narrowing, there were no notable differences in ocular medications. More specifically, 21 of the 31 patients received identical medications in both eyes. Of the remaining 10 patients, 5 were given 1 additional medication in the eye with narrowing, and 5 received 1 additional medication in the unaffected eye. Similarly, there was no statistically significant difference in intraocular pressure between eyes with and without narrowing. The mean ± SD intraocular pressure from the last 3 patient visits in the group of eyes with narrowing was 15.8 ± 4.8 mm Hg vs

Figure 1. Peripapillary focal arteriolar narrowing at the 5-o’clock position in the left eye of a 67-year-old man with primary open-angle glaucoma.

Figure 2. Box plot of mean deviation scores in eyes with and without peripapillary narrowing. The line within the box, the limits of the box, and the upper and lower bars indicate the mean, 25th to 75th percentiles, and 10th to 90th percentiles, respectively.
In subjects with peripapillary focal arteriolar narrowing of the retinal vessels in only one eye, we found that eyes with narrowing had significantly greater visual field defects, characterized by worse MD and CPSD, compared with fellow eyes without narrowing. We have also shown that the degree of constriction does not appear to influence severity of the visual field defect.

This study extends the research that has been done in the area of peripapillary retinal vasculature in patients with glaucoma. In 1989, Jonas et al\textsuperscript{3} showed that the caliber of peripapillary arterioles and veins was significantly smaller in patients with glaucoma compared with healthy controls. More recently, Hall et al\textsuperscript{4} published research showing that eyes with primary open-angle glaucoma display a correlation between decreased peripapillary arteriole diameter and visual field defects in the corresponding hemifield.

In addition, several correlations have been demonstrated between reduced retinal vessel caliber and various morphologic changes indicative of glaucomatous damage, including increased cup-disc ratio, diminution of the neuroretinal rim area, and greater peripapillary atrophy.\textsuperscript{5,6} In 1996, a study by Rankin and Drance\textsuperscript{7} found that peripapillary focal arteriolar narrowing corresponded to an area of peripapillary atrophy in 72.2% of eyes. In previous studies, a correlation had been shown between the location of peripapillary atrophy and that of glaucomatous visual field defects,\textsuperscript{8,9} so it was not surprising when Rankin and Drance found a similar correlation between the position of peripapillary narrowings and the presence of visual field defects in the corresponding hemifield. Although proximal constriction has been related to the presence of visual field defects and optic nerve atrophy, to our knowledge, our study is the first to relate peripapillary narrowing to the severity of disease.

Papastathopoulos and Jonas\textsuperscript{10} proposed that peripapillary focal arteriolar narrowing could signal the progression of glaucomatous disease. In their study, the narrowness of constriction increased significantly in patients with progressive glaucomatous optic neuropathy, whereas the narrowings remained stable in patients with nonprogressive glaucoma. Although we did not find that the degree of constriction correlated with worse visual field defects, the presence of proximal narrowing may indeed be a marker of disease progression.

It remains unclear whether peripapillary narrowings occur secondary to glaucomatous damage or represent a primary pathologic finding that plays a causative role in the disease. One theory proposes that arteriolar narrowing occurs in response to axon loss from the nerve fiber layer secondary to optic atrophy. Such narrowing would be a natural autoregulatory response to the diminished need for blood flow.\textsuperscript{1,11-14}

Table 2. Comparison of Mean Deviation and Corrected Pattern Standard Deviation in Eyes With Severe Peripapillary Focal Arteriolar Narrowing and Eyes With Mild Narrowing\textsuperscript{a}

<table>
<thead>
<tr>
<th></th>
<th>Eyes With Mild Narrowing\textsuperscript{†} (n = 13)</th>
<th>Eyes With Severe Narrowing\textsuperscript{‡} (n = 18)</th>
<th>P Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean deviation, dB</td>
<td>-8.58 ± 8.0</td>
<td>-8.91 ± 8.7</td>
<td>.92</td>
</tr>
<tr>
<td>Corrected pattern standard deviation, dB</td>
<td>6.00 ± 3.4</td>
<td>4.29 ± 3.4</td>
<td>.18</td>
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\textsuperscript{a}Data are presented as mean ± SD unless otherwise indicated. 
\textsuperscript{†}Indicates constrictions graded 1. 
\textsuperscript{‡}Indicates constrictions graded 2 to 4. 
\textsuperscript{§}Determined using an independent 2-tailed t test.

Table 3. Mean Differences in MD and CPSD Between Eyes With Peripapillary Focal Arteriolar Narrowing and Fellow Eyes Without Narrowing: Comparison of Eyes With Severe vs Mild Narrowing

<table>
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<th>Eyes With Mild Narrowing\textsuperscript{†} (n = 13)</th>
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<th>P Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference in MD, dB</td>
<td>3.45 ± 6.10</td>
<td>4.85 ± 8.06</td>
<td>.61</td>
</tr>
<tr>
<td>Mean difference in CPSD, dB</td>
<td>3.03 ± 4.00</td>
<td>1.23 ± 3.00</td>
<td>.16</td>
</tr>
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\textsuperscript{a}Data are presented as mean ± SD unless otherwise indicated. MD indicates mean deviation; CPSD, corrected pattern standard deviation. 
\textsuperscript{†}Indicates constrictions graded 1. 
\textsuperscript{‡}Indicates constrictions graded 2 to 4. 
\textsuperscript{§}Determined using an independent 2-tailed t test.
On the other hand, focal arteriolar narrowing of retinal vessels may play a causative role in the etiology of glaucomatous optic neuropathy by initiating ischemia. Optic nerve blood flow in glaucoma is an active area of research, and numerous studies using different measurement techniques have shown diminished blood flow in glaucomatous eyes.1-10 A recent study found that primary open-angle glaucoma suspects without visual field defects showed similar decreases in optic nerve blood flow to those in patients with advanced glaucoma, suggesting that reduction in blood flow may play an etiologic role.11 Interestingly, Rankin and Drance12 postulated that the absence of tight junctions in areas of peripapillary atrophy could allow leakage of vasoactive substances that contribute to the development of proximal arteriolar constrictions. Areas of peripapillary atrophy have been associated with an increased prevalence of arteriolar constrictions and the absence of tight junctions.13 Finally, it is also possible that vessel constriction and visual field deterioration occur together as a result of another unknown factor or process.

Because peripapillary focal arteriolar narrowing is not specific for glaucoma, it has limited usefulness as a diagnostic tool; however, it may be useful as a marker of disease severity. In patients with early glaucoma, proximal narrowing may be an additional harbinger of advancing glaucomatous disease.

Our study has some limitations. As with any retrospective study, accuracy of data collection and bias are potential sources of error. One potential confounding factor is the possibility that a fundus photograph was taken during an episode of vasospasm and that this constriction might be transient. Rankin and Drance14 proposed that focal narrowing could be caused by vasospasm and described 1 patient in whom narrowing actually resolved with time. However, these authors and others agree that the presence and location of arteriolar narrowing are constant in most patients.15 All of our patients had consistent evidence of narrowing on multiple photographs across time.

When comparing the eyes of patients who exhibit focal arteriolar narrowing of the retinal vessels in only one eye, we found that eyes with narrowing had significantly greater visual field defects. The degree of arteriolar narrowing did not correlate with the severity of visual field defects. By comparing the eyes of a single patient, factors such as age, race, sex, systemic medications, and other diseases are well controlled for. This study relates peripapillary narrowing of retinal arterioles to the severity of glaucomatous damage and supports the idea that proximal narrowing could be a marker for worse visual field status. In the future, it will be important to elucidate whether focal arteriolar narrowing occurs primarily or is secondary to glaucomatous damage. Only then can the significance of this clinical finding be fully understood.

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REFERENCES