Pattern of Vascular Nonperfusion in Retinal Venous Occlusions Occurring Within the Optic Nerve With and Without Optic Nerve Head Swelling

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Objective: To investigate the significance of optic nerve head swelling (ONHS) in relation to the pattern of vascular nonperfusion, visual acuity (VA), and demographic profile in retinal venous occlusions (RVOs) occurring within the optic nerve.

Methods: Cases of RVO occurring within the optic nerve were divided on the basis of the presence (105 cases) or absence (163 cases) of ONHS. This division was performed by examining the color stereo fundus photographs in conditions masked from other clinical parameters. Duration of symptoms before assessment, age, and sex distributions were compared. The vein involved was identified, and the occlusion was confirmed to have occurred within the optic nerve by observing that the vein pierced the lamina cribrosa as a dilated vein. Fluorescein angiographs were examined, and the extent of vascular nonperfusion in the macula and peripheral retina was quantified from grade 1 to grade 4. The extent of break in the perifoveal capillary arcade was graded as 0, less than or equal to 90°, and greater than 90°. Best-corrected VA was assessed using the Snellen chart.

Results: The 2 groups were comparable in terms of the duration of the symptoms before examination. The mean ± SD age was significantly younger in the group with ONHS (58.3 ± 12.9 years, P < .001). Age distribution by sex demonstrated a higher proportion of men younger than 50 years in the ONHS group (19.1% vs 8.6%, P < .01). The group without ONHS involved the papillary vein more frequently (31.3% vs 17.1%, P < .01). The respective proportions of grade 1, 2, 3, and 4 vascular nonperfusion in the macula were 90.5%, 9.5%, 0%, and 0% in the ONHS group, and 62.6%, 14.7%, 13.5%, and 9.2% in the group without ONHS (P < .001). The corresponding proportions for the peripheral retina were 90.4%, 8.7%, 0%, and 1.0% in the ONHS group, and 67.4%, 13.0%, 18.0%, and 6.2% in the group without ONHS (P < .001). In 64.6% of cases with ONHS and 42.9% of cases without, the perifoveal arcade was intact. A break greater than 90° in the perifoveal arcade was present in 12.5% of cases with and 23.6% of cases without ONHS (P < .004). The median VA was significantly better in the ONHS group (6/24 vs 6/48, P < .005).

Conclusions: The RVOs occurring within the optic nerve can be subdivided into 2 distinct groups on the basis of ONHS. The presence of ONHS is associated with younger age, less severe vascular nonperfusion, and better VA. This is consistent with a retrocribrosal site of occlusion, which has access to the pial plexus that can provide collateral channels for retinal venous drainage.
SUBJECTS, MATERIALS, AND METHODS

This study was performed prospectively between January 1976 and December 1990 and considered 1194 consecutive cases referred with a preliminary diagnosis of nondiabetic RVO. Three hundred twenty cases were excluded because the diagnosis of RVO could not be confirmed by the definitions used in this study. Of the remaining 874 cases, 384 occurred in the optic nerve head. Due to media opacification, photophobia, or poor mydriasis, adequate color stereo photographs and fluorescein angiographic studies could only be obtained in 268 cases.

Retinal venous occlusion was defined as a hypoxic retinopathy within the distribution of a significantly obstructed vessel. A significant obstruction of a vein was identified morphologically by its dilated appearance. The occlusion was considered to have occurred within the optic nerve if the obstructed vein entered the lamina cribrosa (LC) as a dilated vein.

All investigations were performed at the initial visit. Fundus photography was performed with a fundus camera (Zeiss FF4; Zeiss, Germany) using Kodachrome 25-color transparency film (Kodak Australasia, Victoria, Australia). Fluorescein angiography was performed with the patient’s informed consent, using black-and-white film (Ilford FP4; Ilford Anitec, Victoria) and printed on transparent contact sheets. In each case the following investigations were included: color photographs and fluorescein angiographs of the affected eye showing the occluded vein and the involved area of the retina, and color stereo photographs of the optic nerve in the affected eye. Best-corrected VA was assessed using a Snellen chart under a standardized condition.

NOMENCLATURE OF RETINAL VENOUS SYSTEM

Sir Stewart Duke-Elder’s classic description of the anatomy of the venous drainage of the retina serves as a basis for using a standard and correct nomenclature for naming the retinal veins. Based on his description, we propose the following scheme for classifying the retinal venous system. The terminal retinal venules are defined as the vessels that feed directly from the capillary bed. Near the ora serrata, the terminal retinal venules bend to form an incomplete ring. The terminal retinal venules drain into retinal venules, which in turn drain into the minor retinal veins. The minor retinal veins converge until one main retinal vein is formed in each quadrant. The superior papillary vein is formed by the union of the superotemporal and superonasal main retinal veins, while the inferior papillary vein is formed by the 2 inferior main retinal veins. The 2 papillary veins join to form the central retinal vein (CRV). In about one fifth of the normal eye, this union takes place within the optic nerve, each papillary vein entering the nerve tissue separately.

QUANTIFICATION OF FLUORESCEIN ANGIOGRAPHS

A single observer (H. K. K.) who was masked from other aspects of the study performed all quantifications. Presence of ONHS was determined by examining the color stereo photographs of the optic disc prior to the review of fluorescein angiographs and without the knowledge of age, sex, or other clinical features of the cases. Optic nerve head swelling was defined as an elevation of the optic nerve head above the surrounding retina, associated with evidence of edema, exudate, or hemorrhage on the optic nerve.

Three morphological patterns of vascular nonperfusion were defined for the purposes of this study. Coarse nonperfusion was defined as closure of individual capillaries with dilatation of adjacent capillaries, resulting in an irregular coarsening of the appearance of the capillary bed (Figure 1). Mosaic nonperfusion was defined as a confluent area of capillary closure bounded by perfused capillaries or venules (Figure 1 and Figure 2). Broad nonperfusion was defined as a confluent area of capillary closure bounded by perfused capillaries or venules (Figure 1 and Figure 2). It was also noted that even in the absence of nonperfusion, the capillary beds may be abnormally dilated (Figure 3).

Based on the morphologic characteristics of vascular nonperfusion, the severity of nonperfusion was graded into 4 levels. In grade 1 nonperfusion, capillary beds were dilated or coarse, with no areas showing mosaic or broad patterns of closure; grade 2, the capillary beds were predominantly dilated or coarse, with smaller areas of mosaic or broad nonperfusion; grade 3, mosaic and broad nonperfusion were predominant, with greater areas of mosaic than broad pattern of closure; and grade 4, mosaic and broad nonperfusion were predominant, with greater areas of broad than mosaic pattern of closure.

Break in the perifoveal capillary arcade was defined as closure of any segment of the innermost capillary loop around the fovea (Figure 4). The extent of break in the perifoveal capillary arcade was measured using a graticule viewed under a high-powered loop. The break in the arcade was graded as 0, less than or equal to 90°, and greater than 90°.

STATISTICAL ANALYSIS

The data were entered into a database management program (Paradox 7.0; Borland International, Scotts Valley, Calif), and statistical analyses were performed using a commercially available statistical package (Statistica version 4.5; Statsoft, Australia). Continuous variables were compared using a 2-tailed, 2-sample parametric test for means, after the normality of distribution was confirmed both qualitatively on histograms and quantitatively by Kolmogorov-Smirnov test. Visual acuity was analyzed by nonparametric analysis, and comparison was performed using the Mann-Whitney U test. Categorical variables were compared using χ² tests.

the 2 subgroups (Kolmogorov-Smirnov, P > .20). The mean ± SD (range) for age was 58.3 ± 12.7 (24-83) years in the ONHS group and 65.1 ± 12.4 (26-94) years in the group without ONHS. The difference in the mean age between the groups with and without ONHS was significant (P < .001). Age distribution categorized by ONHS and sex is shown in Figure 5. There appeared to be a greater proportion of younger men in the group with ONHS (Figure 5).
5, C). The proportion of young men, defined retrospectively as 50 years or younger, was higher in the group with (19.1%) than in the group without (8.6%) ONHS, and the difference was significant ($P = .01$).

**SEX**

There were 161 men (60.1%) and 107 women (39.9%) in this series. The proportion of men was 68 (64.8%) of 105 cases with RVO and ONHS, and in 93 (57.1%) of 163 cases without ONHS. There was no overall statistical difference between the 2 groups in terms of sex.

**ANATOMICAL VEIN INVOLVED**

Of 268 cases, 199 (74.2%) involved the CRV, 63 (23.5%) involved 1 papillary vein, and 6 (2.2%) involved both papillary veins. Occlusion of a papillary vein led to an approximately hemispheric retinal involvement, while CRV occlusion always affected the entire retina. Occlusion of both papillary veins also led to 100% retinal involvement, but 6 cases in this series could be identified as papillary vein occlusions on the basis of the different severity of retinopathy in the respective drainage areas of the papillary veins. **Table 2** gives the proportion of CRV, papillary, and bipapillary occlusions in the 2 subgroups. The proportion of papillary vein occlusion was significantly higher in the group without ONHS (31.3% vs 17.1%, $P = .01$).
EXTENT OF VASCULAR NONPERFUSION

The prevalence of grade 1 to grade 4 nonperfusion in the macula is given in Table 3. There was a higher proportion of grade 1 nonperfusion in the group with ONHS (90.5%) compared with the group without (62.6%), while grade 3 and grade 4 nonperfusion were higher in the group without ONHS. These differences were significant ($P<.001$). The findings were almost identical for the peripheral retina (Table 3, $P<.001$). Almost a quarter of cases without ONHS showed predominantly a mosaic or broad pattern of nonperfusion (grade 3 or grade 4) compared with only 1 case of RVO with ONHS, which showed predominantly a broad pattern of closure in the periphery.

To control for the possible effect of age on the severity of nonperfusion, the analysis was repeated after dividing the cases into age groups of 50 years or younger, 51 to 70 years, and older than 70 years (Table 3). The mean ages were comparable between RVOs with and without ONHS for all age groups ($P>.30$). The trend for higher proportions of grade 3 and grade 4 nonperfusion in RVOs without ONHS continued for both the macula and periphery in all age groups but did not reach statistical significance in the 70 years or older age group.

Of 20 cases of RVO with ONHS occurring in men aged 50 years or younger, 19 had grade 1 nonperfusion, and 1 had a small area of mosaic closure in the macula (grade 2). In 16 of 20 cases, the capillary beds were predominantly dilated, while in the remaining 4 cases, they were predominantly coarse. In contrast, of 14 corresponding cases without ONHS, half had grade 2 to grade 4 nonperfusion. Of 7 cases with grade 1 nonperfusion, 3 were predominantly dilated, and 4 were predominantly coarse.

BREAK IN PERIFOVEAL ARCADE
AND VISUAL ACUITY

The extent of break in the perifoveal arcade could be assessed in 236 cases (88%) (Table 4). There was a trend
for a greater extent of perifoveal arcade disruption in the group without ONHS ($P = .004$).

Table 5 gives the median VA and quartile points in the 2 groups classified by ONHS. The median VA was significantly better in the group with ONHS (6/24 vs 6/48, $P = .005$).

### COMMENT

The percentages of cases that were excluded because of inadequate angiographic studies were similar in the 2 groups, 32% and 29% in the groups with and without ONHS, respectively. The 2 groups are comparable in terms of the duration of symptoms before evaluation.

Lyle and Wybar first described a type of CRV occlusion characterized by mild retinopathy, prominent ONHS, and young age of onset. Several names have been introduced for this entity, including retinal vasculitis and optic disc vasculitis, but it is best known as papillophlebitis. The younger age overall, and male preponderance in patients aged 50 years or younger seen in the group with ONHS, is consistent with these observations.

The difference in vascular nonperfusion between the 2 groups was more marked for the macular and peripheral than for the foveal area. Severe (grade 3 or grade 4) vascular nonperfusion was found in the macula in 23% and in the periphery in 24% of cases with RVO without ONHS (Table 3). In contrast, none of the cases of RVO with ONHS had severe vascular nonperfusion in the macula, and only 1% had severe vascular nonperfusion in the periphery. The extent of break in the perifoveal arcade was greater in the group without ONHS, but this parameter did not separate the 2 groups as clearly as nonperfusion in other areas (Table 4). Significant (>90°) break in the perifoveal arcade was present in 24% of cases without ONHS and in 13% of cases with ONHS. Approximately one third of cases with ONHS showed some degree of disruption in the perifoveal arcade. The break in the perifoveal arcade represents nonperfusion specific to the foveal region. Different factors, such as degree of macular edema, may affect the loss of foveal as opposed to other retinal capillaries.

The progression from a normal to a swollen optic disc could be thought to represent an increase in the severity of the RVO. This article shows clearly that it is the reverse. Optic nerve head swelling in RVO is associated with a better VA and a lesser risk of severe vascular nonperfusion. There is a marked difference in the VA between the 2 groups, with the minimum angle of resolution being twice as large in patients without ONHS (Table 5). The Central Vein Occlusion Study Group has shown that VA at initial examination and amount of nonperfusion are the best predictors of the risk of developing rubeosis. The presence of ONHS, therefore, is likely to indicate a better prognosis. Future studies will be required to show if it is an indicator of a lesser risk not only of having severe vascular nonperfusion but also of progressing to a nonperfused status.

### PATHOGENESIS OF OPTIC NERVE HEAD SWELLING IN RETINAL VENOUS OCCLUSION

Optic nerve head swelling, whether due to inflammation, raised cerebrospinal fluid, or mechanical obstruction, is believed to be caused by the disruption of axoplasmic transport, which leads to accumulation of organelles and axoplasmic debris at the site of the insult. It is likely to be due to the same mechanism in pa-

### Table 2. Comparison of the Rate of Central and Papillary Vein Involvement in Retinal Venous Occlusions With and Without Optic Nerve Head Swelling*

<table>
<thead>
<tr>
<th>ONHS</th>
<th>CRV</th>
<th>PV</th>
<th>Bi-PV</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>87 (82.9)</td>
<td>16 (15.2)</td>
<td>2 (1.9)</td>
<td>.01</td>
</tr>
<tr>
<td>Absent</td>
<td>112 (68.7)</td>
<td>47 (28.8)</td>
<td>4 (2.5)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

*ONHS indicates optic nerve head swelling; CRV, central retinal vein; PV, papillary vein; Bi-PV, bilateral papillary vein; ellipses, not applicable. Values are given as No. (%) except where indicated.

### Table 3. Comparison of the Rate of Grade 1 to Grade 4 Nonperfusions Between Retinal Venous Occlusions With and Without Optic Nerve Head Swelling*

<table>
<thead>
<tr>
<th>Retinal Area</th>
<th>Age Group, y</th>
<th>ONHS</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macula</td>
<td>All Present</td>
<td>95 (90.5)</td>
<td>10 (9.5)</td>
<td>0</td>
<td>0</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>102 (62.6)</td>
<td>24 (14.7)</td>
<td>22 (13.5)</td>
<td>15 (9.2)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤50 Present</td>
<td>23 (95.8)</td>
<td>1 (4.2)</td>
<td>0</td>
<td>0</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>8 (44.4)</td>
<td>4 (22.2)</td>
<td>4 (22.2)</td>
<td>2 (11.1)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;50, ≤70</td>
<td>60 (90.9)</td>
<td>6 (9.1)</td>
<td>0</td>
<td>0</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>55 (64.0)</td>
<td>12 (14.0)</td>
<td>14 (16.3)</td>
<td>5 (6.8)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;70 Present</td>
<td>12 (80.0)</td>
<td>3 (20.0)</td>
<td>0</td>
<td>0</td>
<td>.40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>39 (66.1)</td>
<td>10 (17.0)</td>
<td>3 (5.1)</td>
<td>7 (11.9)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>Periphery</td>
<td>All Present</td>
<td>94 (90.4)</td>
<td>9 (8.7)</td>
<td>0</td>
<td>1 (1.0)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>101 (62.7)</td>
<td>21 (13.0)</td>
<td>29 (18.0)</td>
<td>10 (6.2)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤50 Present</td>
<td>23 (95.8)</td>
<td>1 (4.2)</td>
<td>0</td>
<td>0</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>6 (35.3)</td>
<td>5 (29.4)</td>
<td>6 (35.3)</td>
<td>0</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;50, ≤70</td>
<td>60 (92.3)</td>
<td>4 (6.2)</td>
<td>0</td>
<td>1 (1.5)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>55 (64.0)</td>
<td>11 (12.8)</td>
<td>19 (22.1)</td>
<td>1 (1.2)</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;70 Present</td>
<td>11 (73.3)</td>
<td>4 (26.7)</td>
<td>0</td>
<td>0</td>
<td>.28</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>40 (69.0)</td>
<td>8 (13.8)</td>
<td>2 (3.5)</td>
<td>8 (13.8)</td>
<td>. . .</td>
<td></td>
</tr>
</tbody>
</table>

*ONHS indicates optic nerve head swelling; ellipses, not applicable. Values are given as No. (%) except where indicated.
tients with RVO. Presumably, the venous occlusion causes sufficient hypoxia to disrupt axoplasmic transport at about the level of the LC.

We postulate that if the venous occlusion is located at the LC, the bulk of the venous drainage of the optic nerve head will remain unaffected (Figure 6, A). If axoplasmic stasis is to occur, it will be localized distal to the optic nerve head (ie, on the retina). In contrast, if the occlusion is located in the retrocribrosal space (Figure 6, B), the centripetal venules and capillaries of the optic nerve head distal to the obstruction can no longer drain into the CRV. Furthermore, the luminal pressure of the CRV will become elevated, and the venous drainage from the retina will flow into the optic nerve plexus in a retrograde fashion. As a consequence, the pressure within the optic nerve head capillary plexus will increase and interfere with arterial supply. The resultant ischemia of the optic nerve head could lead to axoplasmic stasis and ONHS. The optic nerve head is particularly susceptible to a rise in the capillary pressure because its main arterial supply via the choroidal circulation is poorly autoregulated.10

OPTIC NERVE HEAD SWELLING AND RETINAL ISCHEMIA

In patients with papillary or CRV occlusion, the presence or absence of ONHS accurately predicts the state of the capillary bed at the time of initial examination. It determines a 24-fold difference in the incidence of severe (grade 3 and grade 4) capillary nonperfusion in the peripheral retina. A large series of patients needs to be followed (for at least 12 months) to see if this is an equally powerful predictor of visual prognosis and risk of rubeosis.

The effect of different sites of occlusion within the optic nerve on retinal ischemia has been investigated experimentally. Fujino et al11 induced severe retinal ischemia by occluding the CRV at the level of the LC. Hayreh,12 obstructing the CRV at the point where it exited the optic nerve, induced little retinopathy. It is likely that the main determinant of retinal ischemia is the availability of collateral channels. The capillaries and venules that normally drain the optic nerve head into the CRV can act as collaterals by diverting retinal venous drainage into the pial plexus and choroidal circulation (Figure 6, B). Access to these collateral channels would require the occlusion to be located behind the LC. If the occlusion is at the LC, the retinal circulation is relatively isolated from these alternative drainage routes (Figure 6, A). The severe ischemia seen in patients without ONHS in this study is consistent with the site of occlusion being at the LC, having limited access to an alternate drainage route.

If an occlusion is behind the LC, the ready access to alternative venous drainage routes via the choroid or

Table 4. Comparison of the Extents of Break in the Perifoveal Capillary Arcade Between Retinal Venous Occlusions With and Without Optic Nerve Head Swelling

<table>
<thead>
<tr>
<th>ONHS</th>
<th>0°</th>
<th>≤90°</th>
<th>&gt;90°</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>62  (64.6)</td>
<td>22  (22.9)</td>
<td>12  (12.5)</td>
<td>. . .</td>
</tr>
<tr>
<td>Absent</td>
<td>60  (42.9)</td>
<td>47  (33.6)</td>
<td>33  (23.6)</td>
<td>.004</td>
</tr>
</tbody>
</table>

*ONHS indicates optic nerve head swelling; ellipses, not applicable. Values are given as No. (%) except where indicated.

Table 5. Comparison of Visual Acuity Between Retinal Venous Occlusions With and Without Optic Nerve Head Swelling

<table>
<thead>
<tr>
<th>ONHS</th>
<th>Median VA</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>6/24</td>
<td>6/60</td>
<td>6/12</td>
<td>.005</td>
</tr>
</tbody>
</table>

*ONHS indicates optic nerve head swelling; VA, visual acuity; ellipses, not applicable.
The pial plexus should reduce the likelihood of severe vascular nonperfusion. The presence of ONHS can only be explained by the site of occlusion being behind the LC. The association of ONHS with a lesser risk of nonperfusion is once again consistent with this postulated retrocribrosal site of occlusion.

Hayreh12 showed that occluding the central retinal artery at the same time led to the retinopathy typically seen in CRV occlusion. This suggests that in the presence of extensive arterial disease in a patient with a retrocribrosal RVO, severe retinal ischemia could occur even when efficient collateral channels are available. In the absence of significant arterial disease, the site of occlusion would have to be closer to the LC, with a lesser access to the alternate drainage routes, for retinopathy to be produced.

The site of occlusion could have other implications. The site of occlusion is likely to be an important causal factor. Ocular pressures, for example, could more readily affect the tissues at the LC rather than behind it, whereas the small disc-at-risk factor seen to play a role in anterior ischemic optic neuropathy would be more likely to affect tissues behind rather than at or in front of the LC. The site of occlusion may also have therapeutic implications. Laser-induced chorioretinal venous anastomosis, for example, may be of less benefit in retrocribrosal RVOs in which there already are efficient collateral channels.

This study has shown that RVOs occurring within the optic nerve can be subdivided into 2 distinct groups on the basis of ONHS. The presence of ONHS is associated with younger age of onset, a less severe vascular nonperfusion, and better VA. Optic nerve head swelling may be an indicator of the site of occlusion within the optic nerve; the absence of swelling suggesting an LC site, and the presence, a retrocribrosal site of occlusion. This has prognostic significance and may have causal and therapeutic implications.

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REFERENCES