Retinal-Vein Occlusion

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors’ clinical recommendations.

A 69-year-old man, a former smoker with a history of hypertension and hyperlipidemia, presents with acute visual loss in his right eye of 2 weeks’ duration. Examination of the eye reveals a visual acuity of 20/60 and a sectoral area of retinal hemorrhages, cotton-wool spots, and swelling in the center of the retina (macular edema). A diagnosis of right-branch retinal-vein occlusion is made. How should he be treated?

The Clinical Problem

Retinal-vein occlusion is a common cause of vision loss in older persons, and the second most common retinal vascular disease after diabetic retinopathy. There are two distinct types, classified according to the site of occlusion. In branch retinal-vein occlusion, the occlusion is typically at an arteriovenous intersection (Fig. 1); in central retinal-vein occlusion, the occlusion is at or proximal to the lamina cribrosa of the optic nerve, where the central retinal vein exits the eye (Fig. 2).

Retinal-vein occlusion has a prevalence of 1 to 2% in persons older than 40 years of age and affects 16 million persons worldwide. Branch retinal-vein occlusion is four times as common as central retinal-vein occlusion. In a population-based cohort study, the 10-year incidence of retinal-vein occlusion was 1.6%. Bilateral retinal-vein occlusion is uncommon (occurring in about 5% of cases), although in 10% of patients with retinal-vein occlusion in one eye, occlusion develops in the other eye over time. Both branch retinal-vein occlusion and central retinal-vein occlusion are further divided into the categories of perfused (non-ischemic) and nonperfused (ischemic), each of which has implications for prognosis and treatment.

Pathogenesis and Risk Factors

The pathogenesis of retinal-vein occlusion is believed to follow the principles of Virchow’s triad for thrombogenesis, involving vessel damage, stasis, and hypercoagulability. Damage to the retinal-vessel wall from atherosclerosis alters rheologic properties in the adjacent vein, contributing to stasis, thrombosis, and thus occlusion. Inflammatory disease may also lead to retinal-vein occlusion by means of these mechanisms. However, evidence of hypercoagulability in patients with retinal-vein occlusion is less consistent. Although individual studies have reported associations between retinal-vein occlusion and hyperhomocysteinemia, factor V Leiden mutation, deficiency in protein C or S, prothrombin gene mutation, and anticardiolipin antibodies, a meta-analysis of 26 studies suggested that only hyperhomocysteinemia and anticardiolipin antibodies have significant independent associations with retinal-vein occlusion.
The strongest risk factor for branch retinal-vein occlusion is hypertension, but associations have been reported for diabetes mellitus, dyslipidemia, cigarette smoking, and renal disease. For central retinal-vein occlusion, an additional ocular risk factor is glaucoma or elevated intraocular pressure, which may compromise retinal venous outflow.

**Natural History and Complications**

Macular edema, with or without macular non-perfusion, is the most frequent cause of vision loss in patients with retinal-vein occlusion. Vision loss may also be due to neovascularization, leading to vitreous hemorrhage, retinal detachment, or neovascular glaucoma.

The natural history of branch retinal-vein occlusion is variable. Many patients with branch retinal-vein occlusion have a good prognosis, with one study showing that half have a return to 20/40 vision or better within 6 months, without treatment. Nevertheless, many patients continue to have poor vision in the affected eye. Among participants enrolled in the Branch Vein Occlusion Study, a randomized trial of the effects of laser treatment for branch retinal-vein occlusion, only a third of untreated eyes with macular edema and presenting vision of 20/40 or worse improved to better than 20/40 after 3 years. Retinal neovascularization developed in one third of untreated eyes.

The visual prognosis is generally worse for patients with central retinal-vein occlusion, particularly when nonperfused, than in patients with branch retinal-vein occlusion. A systematic review suggested that neovascularization may develop in 20% of eyes and neovascular glaucoma in 60% when nonperfused central retinal-vein occlusion.

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**Figure 1. Branch Retinal-Vein Occlusion in the Superotemporal Quadrant of the Right Eye.**

A fundus photograph (Panel A) shows a sectoral area of dilated veins, retinal hemorrhages (white arrows), cotton-wool spots (black arrows), and retinal edema, and a fluorescein angiogram (Panel B) reveals blockage (white arrows) and leakage of dye (yellow arrows). Optical-coherence tomographic scans (horizontal scan in Panel C and vertical scan in Panel D) show retinal thickening (white arrows), as compared with normal retinal thickness (black arrow), and macular edema (yellow arrows). N–T denotes a nasal-to-temporal cut of the retinal scan, and I–S an inferior-to-superior cut.
Conclusion is present. In addition, in one third of eyes initially classified as having perfused central retinal-vein occlusion, the occlusion may become nonperfused within the first year. Visual acuity at the time of presentation is a strong indicator of the ultimate quality of the patient’s vision. In the Central Vein Occlusion Study, a randomized trial of the use of laser treatment for central retinal-vein occlusion, 65% of patients’ eyes maintained 20/40 vision or better if acuity at the time of presentation was 20/40 or better, but only 1% achieved this level if acuity was initially 20/200 or worse.

Despite its associations with vascular risk factors, retinal-vein occlusion does not appear to be an independent risk factor for death from cardiovascular causes. In a pooled analysis of two population-based studies, retinal-vein occlusion was not independently associated with increased cardiovascular mortality, although a post hoc analysis revealed an association among persons younger than 70 years of age.

**Strategies and Evidence**

**Diagnosis and Assessment**

Patients with retinal-vein occlusion typically present with sudden, unilateral, painless loss of vision. The degree of vision loss depends on the extent of retinal involvement and on macular-perfusion status. Some patients with branch retinal-vein occlusion report only a peripheral visual-field defect.

Retinal-vein occlusion has a characteristic appearance on fundus examination. In branch retinal-vein occlusion, there is a wedge-shaped area in which retinal vascular signs (hemorrhages, cotton-wool spots, edema, and venous...
Dilatation and tortuosity arise from an arteriovenous crossing, usually in the superotemporal quadrant (Fig. 1A). In central retinal-vein occlusion, extensive retinal signs, with dilated and tortuous veins, are seen in all quadrants, often along with optic-disc edema (Fig. 2A).

The diagnosis of retinal-vein occlusion is usually made on the basis of the clinical examination alone. Nonperfused central retinal-vein occlusion is suggested by vision that is worse than 20/200, a relative afferent pupillary defect, and the presence of cotton-wool spots and large, confluent hemorrhages. Fundus fluorescein angiography (Fig. 1B and 2B) is commonly performed to assess the severity of macular edema and perfusion status. Optical-coherence tomography is a noninvasive imaging technique used to quantify macular edema and assess treatment response (Fig. 1C, 1D, 2C, and 2D).

Evaluation of patients with retinal-vein occlusion should include a detailed history taking, clinical assessment, and laboratory investigations to check for the presence of cardiovascular risk factors (Table 1). Although evidence is lacking to show that treatment of hypertension and other conditions associated with cardiovascular disease can alter the visual prognosis for patients with retinal-vein occlusion, this condition should be considered end-organ damage, with appropriate risk-management strategies routinely instituted. Tests for coagulation abnormalities (Table 1) are commonly performed in selected patients, such as those younger than 50 years of age or those with bilateral retinal-vein occlusion, although evidence is lacking to indicate that coagulation disorders are more common in these patients.

**Management**

Until recently, laser photocoagulation was the only treatment supported by data from high-quality randomized trials; data are now also available from several trials assessing the use of intraocular glucocorticoids and agents inhibiting vascular endothelial growth factor (VEGF). These more recent treatment options are increasingly being used in clinical practice. (For summaries of the recommendations for the management of branch retinal-vein occlusion and central retinal-

<table>
<thead>
<tr>
<th>Table 1. Assessment of Cardiovascular Risk in Patients with Retinal-Vein Occlusion.</th>
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<tbody>
<tr>
<td><strong>History and clinical assessment</strong></td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Dyslipidemia</td>
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<tr>
<td>Cardiovascular disease (e.g., stroke, coronary artery disease, peripheral artery disease)</td>
</tr>
<tr>
<td>Medications (e.g., oral contraceptives, diuretics)</td>
</tr>
<tr>
<td>Hypercoagulable states and hyperviscosity syndromes (e.g., leukemia, polycythemia vera)</td>
</tr>
<tr>
<td><strong>Routine investigations</strong></td>
</tr>
<tr>
<td>Complete blood count</td>
</tr>
<tr>
<td>Renal function (levels of serum electrolytes, urea, creatinine)</td>
</tr>
<tr>
<td>Fasting serum levels of glucose and glycated hemoglobin</td>
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<tr>
<td>Fasting levels of lipids</td>
</tr>
<tr>
<td><strong>Additional investigations (consider in select cases, such as in patients who are younger than 50 years of age, who have bilateral retinal-vein occlusion, or who may have thrombophilic or coagulation disorders)</strong></td>
</tr>
<tr>
<td>Homocysteine levels</td>
</tr>
<tr>
<td>Levels of functional protein C and protein S</td>
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<tr>
<td>Antithrombin III levels</td>
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<tr>
<td>Antiphospholipid antibodies — lupus anticoagulant, anticardiolipin antibodies</td>
</tr>
<tr>
<td>Activated protein C resistance — polymerase-chain-reaction assay for factor V Leiden mutation (R506Q)</td>
</tr>
<tr>
<td>Factor XII</td>
</tr>
<tr>
<td>Prothrombin gene mutation (G20210A)</td>
</tr>
</tbody>
</table>
vein occlusion, see Tables 2 and 3, respectively.

For the outcomes of trials conducted to gauge the effects of various treatments on each condition, see the Supplementary Appendix, available with the full text of this article at NEJM.org.)

**Branch Retinal-Vein Occlusion**

**Laser Treatment**

Grid laser photocoagulation is used for the treatment of macular edema resulting from branch retinal-vein occlusion, and scatter laser photocoagulation is used for the prevention and treatment of neovascularization. In the Branch Vein Occlusion Study,\(^\text{17,18}\) which included patients with branch retinal-vein occlusion and macular edema in one or both eyes (a total of 139 eyes were studied), eyes treated with grid laser photocoagulation were almost twice as likely as untreated eyes to enable patients to read two additional lines on an eye chart at 3 years (65% vs. 37%).\(^\text{17}\) However, in some patients, poor vision persisted despite treatment; vision in 40% of treated eyes was worse than 20/40 and that in 12% of treated eyes was worse than 20/200 at 3 years. In eyes with extensive nonperfusion, scatter laser photocoagulation markedly reduced the risks of retinal neovascularization (12%, vs. 22% in controls) and vitreous hemorrhage (29% vs. 60%).\(^\text{18}\)

Glucocorticoids

Case series have suggested that intravitreal injection of triamcinolone acetonide may be useful for the treatment of macular edema in patients with branch retinal-vein occlusion.\(^\text{33}\) However, the use of this treatment was not supported by the Standard Care versus Corticosteroid for Retinal Vein Occlusion (SCORE) Study, a randomized trial in which 411 patients with branch retinal-vein occlusion and vision loss from macular edema were treated with intravitreal injection of preservative-free triamcinolone acetonide (1 mg or 4 mg, injected as frequently as every 4 months) or standard care (grid laser treatment of eyes without dense macular hemorrhage).\(^\text{34}\) From baseline to

**Table 2. Recommendations for the Management of Branch Retinal-Vein Occlusion.**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Guidelines</th>
<th>Evidence*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular grid laser photocoagulation</td>
<td>Associated with reduced macular edema and improved vision in patients with macular edema and visual acuity ≤20/40</td>
<td>A-I</td>
<td>May not be effective in presence of macular ischemia</td>
</tr>
<tr>
<td>Scatter laser photocoagulation</td>
<td>Recommended for treatment of ischemic retina if retinal or disk neovascularization is also present</td>
<td>A-I</td>
<td></td>
</tr>
<tr>
<td>Intravitreal injection of triamcinolone acetonide</td>
<td>No more effective than macular grid laser photocoagulation in improving visual acuity in patients with macular edema from branch retinal-vein occlusion and associated with a higher risk of adverse events</td>
<td>A-I</td>
<td></td>
</tr>
<tr>
<td>Intravitreal injection of ranibizumab</td>
<td>Associated with greater improvement in visual acuity, as compared with sham injection, over 12-mo period in patients with macular edema from branch retinal-vein occlusion</td>
<td>A-II</td>
<td>May be administered monthly in 0.5-mg doses, depending on persistence or recurrence of macular edema</td>
</tr>
<tr>
<td>Intravitreal dexamethasone implant</td>
<td>Associated with more rapid improvement in visual acuity than sham implant in patients with macular edema from branch retinal-vein occlusion</td>
<td>B-II</td>
<td>May be administered in 0.7-mg doses every 6 mo, depending on persistence or recurrence of macular edema; contraindicated in patients with advanced glaucoma</td>
</tr>
<tr>
<td>Hemodilution</td>
<td>Not recommended for routine use to improve visual acuity or prevent neovascularization</td>
<td>B-III</td>
<td></td>
</tr>
<tr>
<td>Pars plana vitrectomy with adventitial sheathotomy</td>
<td>Not routinely recommended to improve visual acuity or prevent neovascularization</td>
<td>B-III</td>
<td></td>
</tr>
<tr>
<td>Ticlopidine, troxerutin</td>
<td>Not routinely recommended to improve visual acuity or prevent neovascularization</td>
<td>B-III</td>
<td></td>
</tr>
</tbody>
</table>

* For the ranking of the importance of the recommendation with respect to the clinical outcome, A denotes most important or critical for a good clinical outcome and B moderately important; for the strength of the evidence, I denotes strong evidence in support of the recommendation, II strong evidence in support of the recommendation but lacking in some respects (e.g., longer-term efficacy or safety uncertain), and III insufficient evidence to provide support for or against the recommendation.
1 year, the rate of the primary outcome — the proportion of eyes with an improvement in visual acuity that enabled patients to read 15 or more additional letters (or 3 lines) on an eye chart — was similar among the three groups (27% in the group treated with the 4-mg dose of triamcinolone, 26% in the group treated with the 1-mg dose, and 29% in the control group). Adverse events — principally, elevated intraocular pressure and progression of cataracts — were more frequent in the groups treated with triamcinolone. The percentage of eyes treated with glaucoma medications was 41% in the group receiving 4 mg of triamcinolone, 8% in the group receiving 1 mg, and 2% in the control group; for cataract progression, the percentages were 35%, 25%, and 13%, respectively.

An alternative glucocorticoid, dexamethasone, was evaluated in a randomized trial involving 1267 patients who had vision loss owing to macular edema caused by branch retinal-vein occlusion or central retinal-vein occlusion. The primary end point — the time required to achieve a visual-acuity gain of 3 lines or more on an eye chart — was significantly shorter among patients receiving dexamethasone (in a dose of 0.7 mg or 0.3 mg) than among patients who received a sham injection. The proportion of eyes with this degree of improvement was also significantly higher in both dexamethasone groups than in the placebo group at 1 month and 3 months but not at the prespecified time point of 6 months. Dexamethasone showed similar benefits in preplanned subgroup analyses of branch and central retinal-vein occlusion, although details on the extent of improvement in visual acuity at 3 and 6 months were not provided. However, the proportion of eyes in

### Table 3. Recommendations for the Management of Central Retinal-Vein Occlusion.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Guidelines</th>
<th>Evidence &amp; Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scatter laser photocoagulation</td>
<td>Not recommended for patients without neovascularization unless regular follow-up is not possible</td>
<td>A-I</td>
</tr>
<tr>
<td></td>
<td>Recommended for patients with anterior-segment neovascularization</td>
<td>A-I</td>
</tr>
<tr>
<td>Macular grid laser photocoagulation</td>
<td>Not recommended for treatment of macular edema from central retinal-vein occlusion</td>
<td>A-I</td>
</tr>
<tr>
<td>Intravitreal injection of triamcinolone acetonide</td>
<td>Associated with greater improvement in visual acuity, as compared with observation, in patients with macular edema from central retinal-vein occlusion</td>
<td>A-I May be administered every 4 mo in 1-mg doses, depending on persistence or recurrence of macular edema</td>
</tr>
<tr>
<td>Intravitreal injection of ranibizumab</td>
<td>Associated with greater improvement in visual acuity, as compared with sham injection, over 12-mo period in patients with macular edema from central retinal-vein occlusion</td>
<td>A-II May be administered every mo in 0.5-mg doses, depending on persistence or recurrence of macular edema</td>
</tr>
<tr>
<td>Intravitreal dexamethasone implant</td>
<td>Associated with more rapid improvement in visual acuity, as compared with sham implant, in patients with macular edema from central retinal-vein occlusion</td>
<td>B-II May be administered in 0.7-mg doses every 6 mo depending on persistence or recurrence of macular edema; contraindicated in patients with advanced glaucoma</td>
</tr>
<tr>
<td>Laser-induced chorioretinal anastomosis</td>
<td>May improve visual acuity in patients with nonperfused central retinal-vein occlusion but may be associated with significant ocular complications</td>
<td>B-II</td>
</tr>
<tr>
<td>Hemodilution</td>
<td>May improve visual outcome in some patients if performed as inpatient procedure following a protocol with a statistically relevant clinical outcome</td>
<td>B-II Difficult to generalize recommendation due to variations in protocols (e.g., inpatient and outpatient) and use of different agents</td>
</tr>
<tr>
<td>Ticlopidine, troxerutin, epoprostenol</td>
<td>Not routinely recommended to improve visual acuity or prevent neovascularization</td>
<td>B-III</td>
</tr>
</tbody>
</table>

* For the ranking of the importance of the recommendation with respect to the clinical outcome, A denotes most important or critical for a good clinical outcome and B moderately important; for the strength of the evidence, I denotes strong evidence in support of the recommendation, II strong evidence in support of the recommendation but lacking in some respects (e.g., longer-term efficacy or safety uncertain), and III insufficient evidence to provide support for or against the recommendation.
which elevated intraocular pressure developed
was higher with dexamethasone treatment than
with the sham injection (4% for both dexameth-
asone doses vs. 0.7%, P<0.002). Cataract rates
did not differ significantly among the groups at
6 months.

Anti-VEGF Agents
Ranibizumab and bevacizumab are anti-VEGF
agents that are widely used in the treatment of
neovascular age-related macular degeneration.36,37
Patients with retinal-vein occlusion have higher
vitreous VEGF levels than patients with unaffected
eyes,38 and case series have suggested beneficial
effects when ranibizumab or bevacizumab is used
for the treatment of retinal-vein occlusion.39-42 In
the study of Ranibizumab for the Treatment of
Macular Edema following Branch Retinal Vein
Occlusion (BRAVO), 397 patients who had macu-
lar edema as a result of branch retinal-vein occlu-
sion were randomly assigned to receive intraocu-
lar injections of 0.3 mg or 0.5 mg of ranibizumab
or sham injections, and both groups receiving
ranibizumab had better visual outcomes than the
sham-injection group.43 The primary outcome,
mean improvement in visual acuity (the number of
additional lines that could be read on an eye
chart) at 6 months, was 3 lines in both ranibizu-
mb groups as compared with 1 additional line in
the sham-injection group. The gain of an addi-
tional 3 lines (≥15 letters) occurred at a rate of
61% in the group receiving 0.5 mg of ranibizumab
and 55% in the group receiving 0.3 mg, as com-
pared with 29% in the control group (P<0.001 for
both comparisons with controls). There were no
significant differences in the incidence of sys-
temic vascular events, including stroke, among
the three groups. After 6 months, all patients (in-
cluding controls) who had a visual acuity of 20/40
or worse or who had persistent macular edema
were eligible to receive injections of ranibizumab.
At 12 months, the improvements in vision gained
by patients who had been randomly assigned to
one of the ranibizumab groups were maintained,
whereas controls who were subsequently treated
with ranibizumab had a mean visual improve-
ment of 12 letters (>2 lines) from baseline.

Central Retinal-Vein Occlusion
Laser Treatment
Grid laser photocoagulation does not help to re-
store vision loss from macular edema in patients
with central retinal-vein occlusion. In the Central
Vein Occlusion Study, patients (155 eyes) with
macular edema caused by central retinal-vein oc-
closure and vision of 20/50 or worse had no sig-
nificant improvement in vision after 3 years of
treatment with grid laser therapy, although fluo-
rescein angiographic leakage was reduced.44 In
the same study, scatter laser photocoagulation
decreased the risk of neovascular glaucoma
among patients with iris neovascularization.20

Chorioretinal Venous Anastomosis
Chorioretinal venous anastomosis, a procedure in
which a bypass for the venous obstruction is cre-
ated with the use of laser therapy, has been sug-
gested for patients with perfused central retinal-
vein occlusion.44 In a randomized trial comparing
the use of laser-induced chorioretinal venous
anastomosis with conventional care in 113 pa-
tients with perfused central retinal-vein occlu-
sion, visual acuity did not change in laser-treated
eyes, but in conventionally treated eyes, there was
a loss of 8 letters (nearly 2 lines) from baseline at
18 months (P = 0.03). However, laser-related neo-
vascularization developed in 20% of laser-treated
eyes, and vitrectomy for vitreous hemorrhage
was performed in 10%. Thus, the potential bene-
fit of chorioretinal anastomosis in perfused cen-
tral retinal-vein occlusion must be weighed
against the risk of clinically significant ocular
complications.

Glucocorticoids
Intravitreal injection of triamcinolone was evalu-
ated in the SCORE Study in 271 patients with cen-
tral retinal-vein occlusion and vision loss due to
macular edema.45 At 1 year, improvement in vi-
sual acuity, defined as the ability to read an ad-
ditional 15 letters (3 lines) or more on an eye
chart, occurred in 27% of patients receiving 1 mg
of triamcinolone, 26% of those receiving 4 mg,
and 7% of controls (P = 0.001 for both compari-
sions with controls). Rates of adverse events were
similar to those among the patients with branch
retinal-vein occlusion in the SCORE Study.44 The
study of intravitreal injection of dexamethasone
through an implant was associated with a short-
er time to achieve a gain in acuity of 15 letters
on an eye chart in patients with central retinal-
vein occlusion, as well as in those with branch
retinal-vein occlusion, as discussed above.35 In
both the triamcinolone and dexamethasone stud-
ies, elevated intraocular pressure was a significant adverse event for patients receiving these drugs.

**Anti-VEGF Agents**

Ranibizumab and bevacizumab are widely used in the treatment of central retinal-vein occlusion, as well as in the treatment of branch retinal-vein occlusion. In the Ranibizumab for the Treatment of Macular Edema after Central Retinal Vein Occlusion (CRUISE) trial, which included 392 patients with central retinal-vein occlusion and macular edema, the proportion of patients with clinically significant improvement in visual acuity was higher in the ranibizumab groups than in the sham-injection group (46% of patients receiving 0.3 mg of ranibizumab and 48% of those receiving 0.5 mg vs. 17% of those undergoing sham injection). Like the BRAVO trial, which assessed the same ranibizumab intervention in patients with branch retinal-vein occlusion and in those with central retinal-vein occlusion, the CRUISE study showed no significant between-group differences in the incidence of systemic vascular events among the patients with central retinal-vein occlusion, and the vision gain with ranibizumab treatment was maintained at 12 months.

**Areas of Uncertainty**

Although retinal-vein occlusion is much more common in persons older than 50 years of age, it can also arise in younger persons with no identifiable risk factors. In younger patients, retinal-vein occlusion may have a different pathogenesis, but it is not clear whether systemic coagulation abnormalities are more common in such patients.

Trials of treatments with intraocular glucocorticoid and anti-VEGF agents have had relatively short periods of follow-up. Longer-term trials are needed to determine whether visual gains will be maintained after 1 year, to establish optimal dosing regimens, and to ascertain the risks of these therapies. In some trials, treatment was delayed to allow for spontaneous improvement; thus, it is not clear how different treatments would compare if used earlier in the course of disease.

In post hoc analyses of two trials addressing neovascular age-related macular degeneration, rates of nonocular hemorrhage, including cerebral hemorrhage, were higher among patients treated for 2 years with monthly intravitreal injections of ranibizumab than among controls (7.8% vs. 4.2%, P = 0.01). Although an increased rate of vascular events was not identified in trials of intraocular anti-VEGF agents, more data are needed to assess whether anti-VEGF treatment increases the risk of cardiovascular events, particularly stroke, in patients with retinal-vein occlusion.

Data are lacking from randomized trials comparing glucocorticoids and anti-VEGF therapies head to head and assessing the effects of various combination therapies (e.g., laser plus anti-VEGF therapy). Most trials have largely excluded patients with poor visual acuity and nonperfused retinal-vein occlusion, and it is unclear what type of treatment is appropriate for these patients.

Other systemic therapies have been tried (e.g., hemodilution, streptokinase, and anticoagulants such as troxerutin and ticlopidine), as have surgical approaches (e.g., radial optic neurotomy, performed to improve venous outflow at the optic disc, and vitrectomy with arteriovenous sheathotomy, performed to relieve venous compression at the arteriovenous junctions), but these treatments have not been rigorously studied. Surgical procedures are increasingly being replaced by intraocular injections, which can be given in a physician’s office.

**Guidelines from Professional Societies**

The United Kingdom Royal College of Ophthalmologists has published guidelines for the management of retinal-vein occlusion, but these guidelines do not take into account data from recent clinical trials.

**Conclusions and Recommendations**

The patient described in the vignette has a superotemporal branch retinal-vein occlusion with macular edema. We recommend a thorough ocular evaluation, including the use of fundus fluorescein angiography to assess macular perfusion and leakage and optical coherence tomography to quantify macular edema. Systemic evaluation by the patient’s general physician and appropriate management of modifiable cardiovascular risk factors (e.g., hypertension and hyperlipidemia) are
indicated. We do not recommend further workup for coagulation abnormalities in this patient. We would discuss with the patient the risks and potential benefits of grid laser photoocoagulation or intraocular injections of anti-VEGF agents. The advantages of using grid laser for first-line treatment of branch retinal-vein occlusion include the availability of longer-term data from clinical trials showing improvement in visual acuity, lower rates of adverse effects, and lower costs with this treatment than with anti-VEGF therapy. In selected cases (e.g., dense macular hemorrhage that precludes the use of laser therapy), we would consider intraocular injection of an anti-VEGF agent for first-line treatment; we would inform the patient of the increased risk of arterial thromboembolic events. Treatment with a dexamethasone implant is another option, but evidence is lacking to demonstrate an improvement in visual acuity beyond 3 months. The patient should be monitored closely for signs of neovascularization (e.g., new vessels or vitreous hemorrhage), which would require scatter laser photoocoagulation.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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