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Retinal Vein Occlusions Preferred Practice Pattern®

Published by Elsevier Inc.

http://dx.doi.org/10.1016/j.ophtha.2019.09.029
ISSN 0161-6420/19

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September 7, 2019

Preferred Practice Pattern® guidelines are developed by the Academy's H. Dunbar Hoskins Jr., MD Center for Quality Eye Care without any external financial support. Authors and reviewers of the guidelines are volunteers and do not receive any financial compensation for their contributions to the documents. The guidelines are externally reviewed by experts and stakeholders before publication.

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RETINA/VITREOUS PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The Retina/Vitreous Preferred Practice Pattern® Panel members wrote the Retinal Vein Occlusions Preferred Practice Pattern® (PPP) guidelines. The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

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We thank our partners, the Cochrane Eyes and Vision US Satellite (CEV@US), for identifying reliable systematic reviews that we cite and discuss in support of the PPP recommendations.

The Preferred Practice Patterns Committee members reviewed and discussed the document during a meeting in June 2019. The document was edited in response to the discussion and comments.

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The Retinal Vein Occlusions PPP was then sent for review to additional internal and external groups and individuals in July 2019. All those returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Retina/Vitreous Preferred Practice Pattern Panel reviewed and discussed these comments and determined revisions to the document.

FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at www.cmss.org/codeforinteractions.aspx), relevant relationships with industry are listed. The Academy has Relationship with Industry Procedures to comply with the Code (available at http://one.aao.org/CE/PracticeGuidelines/PPP.aspx). A majority (88%) of the members of the Retina/Vitreous Preferred Practice Pattern Panel 2018–2019 had no financial relationship to disclose.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2019 are available online at www.aao.org/ppp..

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Background:

Retinal vein occlusion (RVO) occurs when there is partial or complete obstruction of a retinal vein, and it is classified by the location of the occlusion. An obstruction of the retinal vein at or posterior to the optic nerve head is a central retinal vein occlusion (CRVO), and complete or partial obstruction at a branch or tributary of the central retinal vein is a branch retinal vein occlusion (BRVO).

Vision loss associated with a vein occlusion usually occurs from macular ischemia or edema, retinal hemorrhages, vitreous hemorrhage, and epiretinal membrane formation. Major risk factors for RVO includes older age (over 40 years of age), arteriosclerosis, systemic arterial hypertension, and diabetes. Specific risk factors associated with BRVO and CRVO are detailed in this Preferred Practice Pattern (PPP). The recommendations of this PPP are based on Cochrane-identified reliable systematic reviews.

Rationale for treatment:

Macular edema may complicate both CRVOs and BRVOs. The first line of treatment for associated macular edema is anti-vascular endothelial growth factors (anti-VEGFs). Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation surgery in BRVO has a potential role in treatment.

Patients who develop iris neovascularization or retinal neovascularization following a CRVO, peripheral panretinal photocoagulation (PRP) treatment is advised. Note, PRP may decrease progression of iris neovascularization and may prevent neovascular glaucoma. Anti- VEGF can be used in an adjunctive manner if angiogenesis continues after PRP.

Care Process:

Patient outcome criteria are to improve or stabilize visual function and vision-related quality of life, detection and treatment of neovascular complications and macular edema, and control of blood pressure, diabetes and blood glucose, and other risk factors through direct communication and coordination of care with the patient's primary care physician. Patients under evaluation for RVO should undergo thorough medical history, ocular exam, and appropriate retinal imaging as needed.

Management recommendations are detailed in this PPP, which includes surgical management and follow-up evaluation. Due to the complexities of the diagnosis and treatment for RVO, the ophthalmologist should be familiar with the specific recommendations of relevant clinical trials. Ophthalmologists should involve primary care physicians of RVO patients as part of their management for systemic conditions.

OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern® guidelines that **identify characteristics and components of quality eye care.** Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern® guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

These documents provide guidance for the pattern of practice, not for the care of a particular individual. While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

Preferred Practice Pattern® guidelines are not medical standards to be adhered to in all individual situations. The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved US Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients' needs are the foremost consideration.

All Preferred Practice Pattern® guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the approved by date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies. The Academy has Relationship with Industry Procedures (available at www.aao.org/about-preferred-practice-patterns) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. The intended users of the Retinal Vein Occlusions PPP are ophthalmologists.

METHODS AND KEY TO RATINGS

Preferred Practice Pattern® guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network[1] (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation[2] (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.[3]

- All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- To rate individual studies, a scale based on SIGN[1] is used. The definitions and levels of evidence to rate individual studies are as follows:

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

- Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE[2] as follows:

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

- Key recommendations for care are defined by GRADE[2] as follows:

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced

- The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel to be of particular importance to vision and quality of life outcomes.
- All recommendations for care in this PPP were rated using the system described above. Ratings are embedded throughout the PPP main text in italics.
- Literature searches to update the PPP were undertaken in March 2018 and June 2019 in PubMed and the Cochrane Library. Complete details of the literature searches are available online at www.aao.org/ppp.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

The prognosis of retinal vein occlusions (RVOs) varies according to the site of the occlusion and the type of occlusion (ischemic or nonischemic). In general, more-distal RVOs with less occlusion have a better prognosis than more-proximal RVOs with greater ischemia.

Central retinal vein occlusions (CRVOs) and hemi-CRVOs have clinically similar courses. They are associated with glaucoma and have a higher risk of anterior segment neovascularization and neovascular glaucoma. Branch retinal vein occlusions (BRVOs) and hemiretinal vein occlusions have a visible arterial-venous crossing where the occlusion occurs.

Macular edema may complicate both CRVOs and BRVOs. The first line of treatment for associated macular edema is anti-vascular endothelial growth factors (anti-VEGFs). Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation surgery in BRVO has a potential role in treatment.

Optimizing control of systemic arterial hypertension, diabetes, serum lipid levels, and intraocular pressure (IOP) to control glaucoma are all important in the management of systemic risk factors, as is communicating end-organ damage to the primary care provider.

INTRODUCTION

DISEASE DEFINITION

Retinal vein occlusion (RVO) is the second most common retinal vascular disorder following diabetic retinopathy and is often associated with vision loss.[4] Retinal vein occlusion occurs when there is a partial or complete obstruction of a retinal vein, and it is classified by the location of the occlusion. An obstruction of the retinal vein at or posterior to the optic nerve head is referred to as a central retinal vein occlusion (CRVO), and a complete or partial obstruction at a branch or tributary of the central retinal vein is referred to as a branch retinal vein occlusion (BRVO). An RVO involves either a complete or partial decrease in venous outflow within the retinal circulation with varying degrees of retinal vascular leakage, leading to both macular edema and an increase of intravenous pressure that results in intraretinal hemorrhages.[4] Branch retinal vein occlusions typically occur at an arteriovenous crossing point, where there is a common adventitial sheath, and are more commonly detected in the superior temporal quadrant.[5] The major risk factors for RVO include systemic arterial hypertension, arteriosclerosis, and diabetes.[6]

A hemiretinal vein occlusion (HRVO) can present in different ways. An HRVO is an occlusion occurring at the disc that commonly involves half of the neurosensory retinal venous drainage, either the superior or inferior hemifield. This pattern occurs in 90% of HRVOs.[7] Some HRVO patients may have two distinctive central retinal veins referred to as hemicentral retinal veins; one drains the superior and the other drains the inferior retinal hemisphere. Occlusion of one trunk is referred to as a hemi-CRVO.[8] In general, HRVOs are clinically similar to BRVOs and have a visible occlusion near a branch point. However, hemi-CRVOs are clinically similar to CRVOs—no crossing point is visible and there is increased risk of late-developing iris and angle neovascularization and secondary elevated intraocular pressures (IOPs). Differentiation between an HRVO and a hemi-CRVO is not always possible.

The loss of vision that is associated with a vein occlusion usually occurs from macular ischemia or edema, retinal hemorrhages, vitreous hemorrhage, epiretinal membrane formation, rubeosis iridis, and neovascular glaucoma.[4] Other findings associated with RVOs include retinal arterial macroaneurysm formation and cilioretinal artery occlusions.

It is now known that all vein occlusions are ischemic to varying degrees as the retina drained by the occluded vessels releases hypoxia related factors such as VEGF as described in the paper by Campochiaro et al, thus there is a spectrum of non-perfusion.[9]

PATIENT POPULATION

The patient population includes people over 40 years of age. The most common age range is from the 6th to the 7th decade.[10,11] Retinal vein occlusions are relatively uncommon in individuals under age 40.

CLINICAL OBJECTIVES

- Identify patients at risk for developing RVO
- Encourage management of potential risk factors for both CRVO and BRVO, including optimizing systemic blood pressure and diabetes as well as control of glaucoma and ocular hypertension
- Increase primary care awareness of the higher risk of cardiovascular and stroke complications in patients presenting with RVO
- Monitor for signs of posterior or anterior segment neovascularization and neovascular glaucoma following all RVOs, because nonischemic can become ischemic
- Treat patients who have vision loss or those at risk for vision loss after RVO
- Minimize treatment side effects that might adversely impact vision and/or vision-related quality of life
- Provide or refer the patient for visual rehabilitation services when permanent visual impairment results from the disease

BACKGROUND

PREVALENCE AND INCIDENCE

The prevalence of RVOs is about 0.5% in the 2008 general world population aged 30 years or older and is estimated to affect more than 16 million people worldwide.[11,12] The prevalence appears to be similar in East Asia and in the United States. Branch retinal vein occlusions occur six to seven times more commonly than CRVOs.[13] African Americans have an incidence of CRVO similar to white Americans, and a gender predilection does not seem to exist.[11] The prevalence of RVOs might be lower in East Indians (0.76/100), with a similar six-fold higher prevalence of BRVO compared with CRVO.[14] In a Japanese study, the 9-year incidence was 3% for any RVO, and there was a nine-fold higher rate of BRVO compared with CRVO.[15] The incidence rate is about 48/100,000 person-years in Korea.[16] In the United States, the 5-year incidence rate is 0.8 per 100, whereas the 15-year incidence is 2.3 per 100 for individuals 40 years of age or older at baseline.[14,16] In China, the 10-year incidence rate for those 40 years of age or older at baseline is 1.9 per 100.[13] In a pooled group of 68,751 subjects aged 30 to 101 years from 15 studies standardized to the 2008 world population, there were 5.2 per 1000 for any vein occlusions (CI = 4.4–6.0), 4.42 per 1000 for BRVO (CI = 3.7–5.2) and 0.8 per 1000 for CRVO (CI = 0.6–1.0).[11]

RISK FACTORS

The main risk factor for both CRVO and BRVO is older age. A prior RVO is a risk factor for an RVO in the fellow eye.[12] The chance of a person with a pre-existing CRVO developing a CRVO in the fellow eye is 1% per year.[17] Patients with a BRVO in one eye have a 10% risk of developing an RVO of either type in the fellow eye over 3 years.[18,19] The other major risk factors for BRVO differ from those for CRVO or hemi-CRVO. Risk of BRVO is more likely associated with local vascular factors

(arterial-venous crossing changes) rather than local ocular factors. Risk factors for BRVO include systemic conditions such as arterial hypertension, hyperlipidemia, diabetes, and coronary artery disease.[20,21] Controversy exists regarding the contribution of other hematologic factors, such as factor V Leiden and homocysteinemia, in the development of BRVO. These hematologic factors may be more likely to contribute to the development of CRVO, although there is not uniform agreement. Retinal phlebitis may be associated with BRVO. Risk factors for CRVO include carotid occlusive disease and sleep apnea as well as glaucoma.[22] In selected cases, elevated homocysteine levels have been associated with CRVO. Fifty-eight percent of patients with CRVO onset at an age younger than 50 were found to have a nontraditional risk factor on systemic/laboratory evaluation.[23-25] In a cohort with systemic lupus erythematosus, the incidence of CRVO was 3.5 times higher than in a control population.[26] A recent meta-analysis and systematic review published in Retina suggests patients with any RVO have an increased risk of cardiovascular events and all-cause mortality.[27]

NATURAL HISTORY

A patient with a CRVO is likely to develop macular edema. Additionally, approximately 25% of patients with CRVO will develop iris neovascularization, and occasional patients may develop retinal neovascularization. Patients with a CRVO have a higher mortality rate than controls in an age-adjusted general population. This additional risk is due to a higher prevalence of cardiovascular disease and diabetes.[28]

An extensive study of the natural history of RVO categorized BRVOs as mild, moderate, or marked, based on the level of capillary nonperfusion seen angiographically.[18] Eyes with BRVO and significant capillary nonperfusion can develop retinal neovascularization and vitreous hemorrhage, but they are much less likely to develop neovascular glaucoma than eyes with CRVO or hemi-CRVO. Macula-involving RVOs are usually acutely symptomatic with the sudden onset of visual symptoms, including a decrease in central vision and/or a corresponding visual field defect. If a BRVO does not involve one of the major temporal branch veins or macular veins, symptoms may go unrecognized unless the occlusion is detected during a routine eye examination or complications develop, such as a vitreous hemorrhage from retinal neovascularization. Typically, patients will present with acute visual symptoms in one eye due to macular edema. Early clinical findings include vascular tortuosity, venous dilation of the affected veins, retinal edema, intraretinal hemorrhages, cotton wool spots, and occasionally hard exudates or even retinal detachment in the affected region.[29] Over time, the acute process resolves and the hemorrhages may clear, along with the cotton wool spots. In general, the macular edema persists and is a common cause of visual dysfunction unless appropriately treated. Collaterals may also develop between the retinal venules and the choroidal circulation at the disc following a CRVO and between the superior and inferior retinal veins in a BRVO.

The prognosis for vision loss due to BRVO depends on the degree of nonperfusion and the location of the occlusion.[30] The Branch Vein Occlusion Study (BVOS) Group found a spontaneous improvement in visual acuity by 2 or more lines in 37% of eyes, whereas only 17% had decreased vision. After 3

years of average follow-up, a mean increase in visual acuity of 2.3 lines occurred in the study, and 34% of eyes attained a final visual acuity of 20/40 or better. However, 23% of eyes had a visual acuity of 20/200 or worse. Recovery of visual acuity usually occurs as a result of the development of collateral vessels that help with the venous drainage and subsequent resolution of retinal edema and ischemia.[30] The severity of the occlusion and extent of ischemia are important prognostic factors for the final visual acuity deficit resulting from BRVO.[31]

Long-standing BRVO is usually characterized by minimal intraretinal blood and resolution of cotton wool spots with mild residual venous tortuosity and collateral vessels adjacent to the affected area. Macular edema may persist yet may also resolve over time, leaving secondary retinal pigment epithelial atrophy and suboptimal visual acuity. Macular edema causes a substantial decrease in vision-related quality of life.[30] Epiretinal membrane often develops in eyes affected by BRVO.

RATIONALE FOR TREATMENT

For individuals who develop iris neovascularization or retinal neovascularization following a CRVO, the best treatment is dense peripheral panretinal photocoagulation (PRP).[32] Although PRP does not usually improve the visual acuity, it decreases the risk of progression to iris neovascularization and may prevent neovascular glaucoma. Additionally, anti-vascular endothelial growth factor (anti-VEGF) agents can be used in an adjunctive manner when the complete PRP is insufficient to control angiogenesis.[32,33] Anti-vascular endothelial growth factor agents are commonly used to treat the macular edema, reduce the severity of anterior segment neovascularization, and lower the risk of ocular angiogenesis.[33] Published data estimates the incidence of macular edema in all BRVOs to be 30%.[34]

CARE PROCESS

Patients under evaluation for RVO should undergo thorough medical history, ocular exam, and appropriate retinal imaging as needed. In general, an internist may be involved in the management of patients with a new RVO because of associated systemic risk factors, including diabetes, hypertension, and hyperlipidemia.[35] Comprehensive ocular examination and retinal imaging should do the following: 1) distinguish RVO as either BRVO or CRVO, 2) evaluate for macular edema, 3) estimate the degree of retinal ischemia, and 4) evaluate for retinal and/or iris neovascularization.

In eyes with BRVO and macular edema, anti-VEGF injections,[36-40] focal laser treatment,[30] and intravitreal steroids[41] all have demonstrated therapeutic benefit.[42-44] In eyes with CRVO and macular edema, anti-VEGF[45-55] and intravitreal steroids[56] have demonstrated benefit. Currently, three anti-VEGF agents are used routinely for the treatment of macular edema associated with RVO; two (ranibizumab and aflibercept) are

approved by the U.S. Food and Drug Administration (FDA). Although, bevacizumab remains off-label for ophthalmologic conditions, there is evidence demonstrating its efficacy and safety.[53-55] Intravitreal corticosteroids (triamcinolone and dexamethasone implant) are considered second line because of significant ocular side effects, such as secondary glaucoma and cataract formation.[56]

In patients with a BRVO and neovascularization of the retina, retinal laser photocoagulation surgery in the area of nonperfusion helps to decrease the risk of a vitreous hemorrhage.[57] In patients with CRVO with retinal and/or iris neovascularization, dense peripheral PRP is indicated.[17] Occasionally, initial treatment with an anti-VEGF agent might be helpful for an immediate but nonsustained benefit and may also improve the ability to deliver a complete laser treatment.[33]

PATIENT OUTCOME CRITERIA

Patient outcome criteria include the following:

- Improvement or stabilization of visual function
- Improvement or stabilization of vision-related quality of life
- Detection and treatment of all neovascular complications
- Detection and treatment of macular edema
- Optimal control of blood pressure, diabetes and blood glucose, and other risk factors through direct communication and coordination of care with the patient's primary care physician

DIAGNOSIS

The initial examination of a patient with a RVO includes all relevant aspects of the comprehensive adult medical eye evaluation,[58] with particular attention to those aspects related to retinal vascular disease.

History

An initial history should consider the following elements:

- The location and duration of vision loss
- Current medications
- Medical history (e.g., systemic hypertension, diabetes, hyperlipidemia, cardiovascular disease, sleep apnea, coagulopathies, thrombotic disorders, pulmonary embolus)
- Ocular history (e.g., glaucoma, other ophthalmologic disorders, ocular injections, surgery, including retinal laser treatment, cataract surgery, refractive surgery)

Examination

The initial examination should include the following elements:

- Visual acuity

- Pupillary assessment for a relative afferent pupillary defect that corresponds to the level of ischemia and is also predictive for eyes at risk for neovascularization
- Slit-lamp biomicroscopy, looking carefully for fine, abnormal, new iris vessels
- IOP
- Gonioscopy prior to dilation. This is important to perform, especially in cases of an ischemic CRVO, when there is an elevated IOP or when iris neovascularization risk is high.
- Binocular funduscopic evaluation of the posterior pole
- Examination of the peripheral retina and vitreous. A dilated examination is recommended to ensure an optimal view of the entire retina. Slit-lamp biomicroscopy with appropriate lenses is recommended to evaluate retinopathy of the posterior pole and midperipheral retina. Examination of the far peripheral retina is best performed using indirect ophthalmoscopy. Because treatment is effective in reducing the risk of vision loss, a detailed examination is indicated to assess for the following features that often lead to visual impairment:
  - Macular edema, detected both clinically and/or by using optical coherence tomography (OCT) imaging
  - Signs of ischemia, including neovascularization of the disc or elsewhere, presence of a relative afferent pupillary defect, extensive hemorrhages, venous dilation and tortuosity, and cotton wool spots
  - Optic nerve head neovascularization and/or neovascularization elsewhere
  - Vitreous or preretinal hemorrhage

Diagnostic Tests

If used appropriately, a number of imaging tests may enhance the clinical examination and optimize patient care. The most common tests include the following:

Color and Red-Free Fundus Photography

Fundus photography is also useful for documenting the severity of the retinal findings, the presence of new vessels elsewhere in the retina (NVE), the extent of intraretinal hemorrhages, and new vessels on or near the optic disc (NVD), the response to treatment, and the need for additional treatment at future visits.

Optical Coherence Tomography

Optical coherence tomography provides high-resolution imaging of the macula and is extremely useful to detect the presence and extent of any associated macular edema, vitreoretinal interface changes, and subretinal fluid. It is also useful to detect or distinguish RVO from other macular diseases. Large clinical trials testing anti-VEGF treatment are based largely on using quantifiable OCT measurements rather than the more subjective stereoscopic photographs or clinical examination to evaluate and follow macular edema. In

clinical practice, treatment decisions are commonly based on OCT measurements. For example, the decision to repeat anti-VEGF injections, change therapeutic agents (e.g., intraocular corticosteroids), initiate laser treatment, or even consider vitrectomy surgery is frequently based on both visual acuity and OCT findings. Nevertheless, retinal thickness, even when measured by OCT, is not always consistently correlated with visual acuity.[59]

Optical Coherence Tomography Angiography

Several studies have demonstrated that in eyes with RVO, noninvasive optical coherence tomography angiography (OCTA) is similar to fluorescein angiography (FA) in detecting capillary nonperfusion, enlarged foveal avascular zone, and vascular abnormalities.[60,61] This promising technology is currently limited by image artifacts and limited field of view. Future studies are needed to determine its clinical utility and if it can replace FA in the future.

Fluorescein Angiography

Fluorescein angiography is used to evaluate the extent of the vascular occlusion, the degree of ischemia (ischemic as defined by the CVOS eyes with 10 disc areas of capillary non-perfusion on standard FA vs. nonischemic), and the extent of macular edema. Angiography can identify macular capillary nonperfusion that may explain the associated vision loss as well as the response to therapy. It is a useful technique to distinguish collateral vessels, which do not leak fluorescein in later frames, from retinal neovascularization that is associated with late leakage. It can identify regions of peripheral nonperfusion, helping to guide effective laser treatment or possibly detecting areas of untreated retinal capillary nonperfusion that may explain persistent retinal or disc neovascularization that remains present after prior laser treatment. Recent advances in wide-field FA have enabled its use to evaluate peripheral nonperfusion, yet current data on the benefits of this technique are inconclusive. Some have proposed that the degree of ischemia on wide-field FA can help classify a CRVO as ischemic or nonischemic as well as determine the risk of conversion of a CRVO from nonischemic to ischemic.[62]

As the use of anti-VEGF agents and intraocular corticosteroids has increased for the treatment of macular edema, the use of grid laser treatment has decreased. Therefore, the need for FA has also declined. However, FA remains a valuable tool and should be considered by ophthalmologists who diagnose and treat patients who have retinal vascular disease.

An ophthalmologist who orders an FA must obtain informed consent and be aware of both common and rare potential risks associated with the procedure, including death in about 1/200,000 patients.[63] Each angiography facility should have in place an emergency care plan and a clear protocol to manage known risks and complications. Fluorescein dye crosses the placenta into the fetal circulation,[64] but detrimental effects of fluorescein dye on

a fetus have not been documented. Nevertheless, women of childbearing age should be questioned about the possibility of pregnancy and breast-feeding, and FA should be recommended only when absolutely necessary.

Ultrasonography

Ultrasonography is an extremely valuable diagnostic tool that enables assessment of the anatomic status of the retina in the presence of a vitreous hemorrhage or other media opacity.

Systemic Evaluation

The extent of the systemic evaluation is dependent on the patient's age and medical history. Discussion with the primary care doctor is important, since a patient who has had an RVO is at risk for developing an RVO in the fellow eye and has a higher risk of cardiovascular disease and cerebrovascular accidents.[12,21] Clear guidelines on systemic testing are lacking.

MANAGEMENT

Prevention and Early Detection

There is a strong relationship between BRVO and systemic vascular disorders such as arterial hypertension and peripheral vascular disease. Older age and systemic vascular disorders are the strongest risk factors for RVO.[65] A recent meta-analysis of published studies suggests that 48% of RVO is attributable to hypertension, 20% to hyperlipidemia, and 5% to diabetes.[35] It is known that arteriovenous nicking, ocular perfusion pressure, and focal arteriolar narrowing are related to an increased risk of developing a BRVO.[21,29] Data are inconclusive in determining whether lowering blood pressure and/or serum lipid levels improves visual acuity or the complications from RVO.[35]

Medical and Surgical Management

Consequences of untreated RVOs and vision loss are an economic burden on patients, their family, and society. Anti-VEGF agents, laser and intravitreal steroids are cost-effective for the management of RVOs. The choice of treatment should be individually tailored based on discussion between the patient, family, and physician.[66,67] The current treatment strategies for BRVO target the sequelae of the venous occlusion (i.e., CME and NVD/NVE) rather than to attempt to treat the occlusion itself.

Anti-Vascular Endothelial Growth Factors

Clinical trials have evaluated the efficacy of anti-VEGF agents and/or intravitreal corticosteroid injections.

Multiple level I studies have demonstrated the efficacy of these agents in the treatment of macular edema associated with BRVO.[37-40,51,65] Currently, there are three that are

commonly used in these cases: off-label bevacizumab and FDA-approved ranibizumab, and aflibercept. The double-masked, multicenter, randomized phase 3 clinical trial BRAVO (Ranibizumab for the Treatment of Macular Edema following Branch Retinal Vein Occlusion: Evaluation of Efficacy and Safety) demonstrated efficacy of monthly intravitreal 0.3 or 0.5 mg ranibizumab compared with sham injection in 397 eyes when followed for 6 months. In this trial, monthly intravitreal ranibizumab injections resulted in a gain of 16 (0.3 mg) to 18 letters (0.5 mg) compared with a gain of 7.3 letters in the sham group at month 6; 55% (0.3 mg) to 61% (0.5 mg) of ranibizumab-treated eyes gained at least 15 letters from baseline compared with 29% in the sham group.[38] After 6 months, all eyes were eligible for injections of ranibizumab 0.5 mg as required until month 12. Eyes randomized to initial sham injection and then eligible for ranibizumab 0.5 mg after 6 months demonstrated vision improvement but did not achieve the level of vision gain compared with those eyes that were randomized to ranibizumab initially—demonstrating that delay in treatment can be deleterious.[42] The benefits of ranibizumab seen at 6 months were generally maintained by month 12.[37] The HORIZON trial included all patients who completed the BRAVO trial and entered an open-label multicenter extension trial. Patients were followed quarterly for 12 months with repeat injections of 0.5 mg ranibizumab, used at the investigator's discretion.[51] Approximately half of the eyes in HORIZON achieved resolution of edema and 80% had visual acuity of better than or equal to 20/40. However, approximately half of the eyes enrolled in the HORIZON extension study received grid laser photocoagulation surgery at some point during the study period. These studies used ranibizumab, whereas other smaller, level II studies have demonstrated the efficacy of bevacizumab for BRVO-associated macular edema.[39,40,65] The VIBRANT trial was a randomized double-masked phase 3 trial that demonstrated the efficacy of aflibercept over grid laser treatment for macular edema in BRVO.[36] Two systematic reviews between 2013 and 2016 have confirmed the efficacy of anti-VEGF injections for treatment of macular edema associated with RVO with minimal side effects.[68,69] *(I++, Good quality, Strong recommendation)*

In general, the use of topical povidone iodine is recommended before all intravitreal injections, whereas the use of routine antibiotic eye drops is not recommended.[70] Severe adverse effects of intravitreal injections are uncommon and include infectious endophthalmitis, cataract formation, retinal detachment, and elevated IOP. There are possible systemic risks associated with anti-VEGF treatment; however, a meta-analysis demonstrated no evidence of increased arterial thromboembolic events associated with anti-VEGF treatment.[71] Intraocular pressure elevations are particularly common with the use of intravitreal corticosteroids and the corticosteroid implants. In conclusion, because of the favorable risk-to-benefit profile, anti-VEGF agents are the preferred initial therapy for treatment of macular edema related to BRVO. Either corticosteroids and/or grid laser

treatment should be considered when there is a failure to respond or an inadequate response.

Several randomized controlled trials have also shown the efficacy of anti-VEGF agents in treating macular edema with CRVO.[45,48,52,72] The Ranibizumab for the Treatment of Macular Edema after Central Retinal Vein Occlusion Study: Evaluation of Efficacy and Safety (CRUISE) showed a doubling of the number of letters read following intravitreal ranibizumab compared with sham injections and a decrease in macular edema by OCT imaging.[48] In the Vascular Endothelial Growth Factor [VEGF] Trap-Eye: Investigation of Efficacy and Safety in Central Retinal Vein Occlusion (COPERNICUS) study, intravitreal aflibercept was compared with sham injections; there was a 15-letter gain in 56% of the treated eyes compared with 12% of sham injections.[45] Similar findings were found in the General Assessment Limiting Infiltration of Exudates in central retinal vein Occlusion with VEGF Trap-Eye (GALILEO) study.[52] Intravitreal bevacizumab was compared with sham injections in a randomized trial that found a 15-letter gain in 60% of the treated eyes compared with 20% for sham injections.[49] Subsequent studies, including 3 systematic reviews, have also supported the efficacy of anti-VEGF for treatment of macular edema secondary to CRVO.[42,43,73-75] *(I++, Good quality, Strong recommendation)*

The Study of Comparative Treatments for Retinal Vein Occlusion 2 (SCORE2) comparison of aflibercept to bevacizumab for macular edema from CRVO showed that aflibercept was similar to bevacizumab in mean visual acuity at 6 months (primary outcome).[76] From months 6 to 12, patients in SCORE2 were then stratified based on their response to the original monthly treatment as good, poor, or marginal response. Those with a good response were then given the original treatment drug monthly or on a treat-and-extend protocol basis. Patients in the treat-and-extend protocol received about one to two fewer injections compared with the monthly regimen. However, because of the widths of the confidence intervals on visual acuity at 12 months, caution is advised before concluding that the two regimens yield similar visual outcomes.[77] For eyes classified as poor responders to aflibercept at 6 months, dexamethasone rescue was used.[77] Aflibercept was used for eyes with a marginal response to bevacizumab.[77]

Steroids

There is a role for intravitreal steroids such as triamcinolone, dexamethasone and other corticosteroids that have been shown to be efficacious for macular edema associated with CRVO, yet there are known associated risks of cataracts and glaucoma.[56,72,78]

The SCORE study for BRVO evaluated the use of two doses of intravitreal corticosteroids (triamcinolone 1 mg and 4 mg) versus macular grid laser therapy in 411 eyes randomized to one of the three treatment arms in a 1:1:1 fashion and followed for 12 months.[41] After 1 year, approximately one-third of eyes in the laser treatment group, one-third of eyes in the

triamcinolone1-mg group, and one-third of eyes in the triamcinolone 4-mg group gained 15 or more letters. The mean gain in best-corrected visual acuity was 4 to 5 letters in all groups; however, patients in either of the corticosteroid groups were more likely to develop cataract or elevated IOP than those who received laser treatment. The SCORE recommendations for BRVO were to consider macular grid laser treatment in eyes with BRVO and perfused macular edema leading to vision loss because the efficacy was similar in all treatment arms.

The SCORE CRVO trial included 271 people aged 68 years on average.[56] Seventy-three percent of patients with CRVO had high blood pressure and 23% percent had diabetes. Patients in the corticosteroid medication groups received an average of two injections in the first 12 months of the study.

After 1 year, 27% of patients in the 1-mg group and 26% of patients in the 4-mg group experienced a substantial visual gain of 3 or more lines of visual acuity. Only 7% of patients in the observation group experienced a similar visual gain. Therefore, patients in the corticosteroid treatment groups were much more likely to have a substantial visual gain at 1 year. These results persisted up to 2 years.

However, participants who received the 4-mg dose had the highest rates of cataract formation, cataract surgery, and elevated IOP within the eye, indicating a preference for the 1-mg dose.[56]

The GENEVA study evaluated the use of the intravitreal dexamethasone implant (Ozurdex®, Allergan, Inc., Irvine, CA) in two doses compared with sham injection in eyes with either a CRVO or a BRVO.[79] The study included pooled data from 1131 patients, 34% with CRVO and 66% with BRVO, and showed that in the BRVO eyes treatment with either the 0.35-mg or the 0.7-mg dose implant had no efficacy at 6 months. However, there was significant visual acuity gain at 90 days that was lost at 6 months. Results from an open-label extension beyond 6 months were similar to the initial study, showing visual acuity gains up to 90 days, then loss of a treatment effect at 1 year.[72] Cataract formation and elevated IOP were seen more frequently at 1 year than at 6 months (16% had an elevated IOP of 25 mmHg or greater). The dexamethasone implant was FDA approved in 2009 for the treatment of macular edema due to CRVO and BRVO.

The COBALT study has shown that with retreatment using the dexamethasone implant as often as every 4 months, significant visual acuity gains can be achieved for eyes with macular edema secondary to a BRVO.[80] In fact, mean visual acuity improvement was 18.6 ± 12.9 and 15.3 ± 15.0 letters at 6 and 12 months, respectively. There was a rapid response, with approximately 70% of maximum treatment response seen at 1 week. Incidence of IOP elevation was 18% and cataract incidence was 16% at one year.

A third corticosteroid implant, fluocinolone, has also been shown to be beneficial in the treatment of BRVO-associated macular edema up to 3 years following injection. There were improvements in both edema and visual acuity,[81] but fluocinolone is not yet approved by the FDA for this indication. Glaucoma and cataract formation were reported side effects in this study.

A Cochrane systemic review questioned the results of SCORE because of incomplete outcome data and the GENEVA study because of selective reporting and found that there was insufficient evidence to determine if steroids are beneficial or not.[82] *(I+, Good quality, Strong recommendation)* A meta-analysis found no difference in visual improvement for treatment of macular edema from CRVO with bevacizumab, ranibizumab, aflibercept and triamcinolone. However, steroid and IOP risks associated with steroids make anti-VEGF more favorable as initial therapy.[78] *(I+, Good quality, Strong recommendation)*

Laser Photocoagulation

The BVOS first demonstrated the efficacy of grid laser photocoagulation surgery for macular edema due to BRVO. Patients with BRVO who presented with a visual acuity of 20/40 or worse due to perfused BRVO (retained macular perfusion on FA) with macular edema were randomized to either grid-pattern laser photocoagulation surgery or no treatment. There were more patients who gained at least 2 lines of visual acuity from baseline in the laser photocoagulation surgery group than in the untreated group (65% vs. 37%). Nearly twice as many treated eyes had final visual acuity outcomes greater than 20/40 when compared with untreated eyes. This finding led to the recommendation that grid laser treatment should be considered for eyes with BRVO, macular perfusion, and macular edema with a visual acuity of 20/40 or worse.[30] However, anti-VEGF results in more improvement in visual acuity (see above) than laser and should be the preferred treatment unless there are contraindications to its use. Further, treatment for macular edema should not be delayed. Patients in whom monthly follow-up is difficult may also be managed more easily with laser photocoagulation surgery, with follow-up 3 months after laser. Sectoral PRP is still recommended for neovascularization when complications such as vitreous hemorrhage or iris neovascularization occur.[57] Most recently, clinical trials have shown no added benefit for macular grid or peripheral scatter laser photocoagulation surgery for BRVO. The 2-year BRIGHTER[83] and the 4-year RETAIN[84] studies demonstrated that adding laser to ranibizumab did not result in a better visual outcome or reduce the need for treatment. In the RELATE study, scatter laser to peripheral ischemic areas did not decrease the macular edema.[85]

The Central Vein Occlusion Study (CVOS) did not show any value of focal photocoagulation for macular edema in patients with CRVO.[17] For patients with iris or

angle neovascularization, the CVOS recommended complete peripheral PRP.[17] Currently, anti-VEGFs are being used as an adjunct to treat iris or angle neovascularization. There is no phase 3 clinical trial evidence for this usage.

Follow-up Evaluation

The follow-up evaluation includes a history and examination.

History

A follow-up history should include changes in the following:

- Symptoms
- Systemic status (pregnancy, blood pressure, serum cholesterol, blood glucose)

Examination

- Visual acuity
- Undilated slit-lamp biomicroscopy and gonioscopy with careful iris examination for early iris or angle neovascularization[86] monthly for 6 months in eyes with CRVO and in eyes with ischemic CRVO after discontinuing anti-VEGF to detect neovascularization[17]
- Pupillary assessment for a relative afferent pupillary defect
- IOP
- Stereoscopic examination of the posterior pole after dilation of the pupils[87]
- OCT imaging, when appropriate
- Peripheral retina and vitreous examination, when indicated[88]

PROVIDER AND SETTING

Although the ophthalmologist will perform most of the examination and any associated surgery, certain aspects of data collection may be performed by trained individuals under the ophthalmologist's supervision and review. Because of the complexities of the diagnosis and treatment for retinal vascular occlusion, the ophthalmologist caring for patients with this condition should be familiar with the specific recommendations of relevant clinical trials.[89-104] The American Academy of Ophthalmology has a stated position and a policy statement on the role of the ophthalmologist in the delivery of intravitreal agents.[105] Outside of the United States, there are varying practice patterns.[106-108]

COUNSELING AND REFERRAL

The ophthalmologist should refer patients with an RVO to a primary care physician for appropriate management of their systemic condition and should communicate examination results to the physician managing the patient's ongoing medical care.[35] The risk to the fellow eye should also be communicated to both the primary care provider and the patient.[12,21] An Eye MD Examination Report Form is available from the American Academy of Ophthalmology.[109] Some patients with RVO will

lose substantial vision despite being treated according to the recommendations in this document. Patients whose conditions fail to respond to therapy and those for whom further treatment is unavailable should be provided with proper professional support and offered referral for counseling, vision rehabilitation, or social services as appropriate.[110] Vision rehabilitation helps to restore some functional ability,[111] and patients with functionally limiting postoperative visual impairment should be referred for vision rehabilitation and social services.[110] More information on vision rehabilitation, including materials for patients, is available at www.aao.org/low-vision-and-vision-rehab.

SOCIOECONOMIC CONSIDERATIONS

Very few studies have evaluated the cost/benefit ratio of the various treatment types for RVO. One study evaluated the cost/benefit ratio of treatment methods for macular edema due to various etiologies. The dollars per quality-adjusted life years (QALY) for treatment of BRVO with macular edema ranges between approximately $800 and $26,000 and for CRVO with macular edema it ranges between approximately $1,400 and $16,000. These are cost-effective treatments.[66] The same study also concluded that the benefit conveyed by pharmacologic therapy for visual acuity, although statistically significant, may be modestly beneficial (i.e., 1 line or less of visual acuity gained). This study demonstrates the wide range of cost parameters for macular edema treatment, ranging from a low of $1,326 for laser to $23,119 for a 1-year course of ranibizumab treatment, a 17-fold difference. Costs per visual acuity line-year ranged from $25 to $754.[66] In this analysis, the natural history of BRVO was calculated as 0.23 lines (1.15 letters) of spontaneous improvement and was used for the natural history adjustment. The index study for laser treatment yielded a 1.33-line (6.65 letters) improvement for laser that yielded 1.1 lines (5.5 letters) saved when reduced by the natural history adjustment. Calculations, including similar adjustments for corticosteroids (with triamcinolone), yielded 1.4 lines saved. Lines-saved values calculated for bevacizumab (4.9) and ranibizumab (2.2) had higher values. When looking at the dollars per QALY, this was $824 for bevacizumab versus $1,572 for grid laser, $5,536 for Ozurdex, and $25,566 for ranibizumab. The dollars per line-year saved followed along similar lines, with bevacizumab at $25, grid laser $68, Ozurdex $162, and ranibizumab $754.

A recent study reported on the direct medical costs for treating CRVO and BRVO in working-age and Medicare populations.[67] The authors found that health care utilization and expenditures for patients with BRVO or CRVO were significantly greater than those for control subjects without these diseases at both 1 and 3 years postdiagnosis. Utilization and expenditures were greater in the first year following diagnosis; however, these continued to exceed those of control subjects at 3 years postdiagnosis. The authors felt that the development of RVO is a marker for poorer overall systemic vascular health and increased utilization of medical resources.

APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

Providing quality care
is the physician's foremost ethical obligation, and is
the basis of public trust in physicians.
AMA Board of Trustees, 1986

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
  - The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
  - The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
  - When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
  - The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.

- The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility. They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn respond in an adequate and timely manner.
- The ophthalmologist maintains complete and accurate medical records.
- On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- The ophthalmologist and those who assist in providing care identify themselves and their profession.
- For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.

- Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices or procedures.
- The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

Reviewed by: Council
Approved by: Board of Trustees
October 12, 1988

2nd Printing: January 1991
3rd Printing: August 2001
4th Printing: July 2005

APPENDIX 2. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

Retinal vein occlusion, which include entities with the following ICD-9 and ICD-10 classifications:

	ICD-9 CM	ICD-10 CM
Central retinal vein occlusion	362.35	H34.811 H34.812 H34.813
Venous tributary (branch) occlusion	362.36	H34.831 H34.832 H34.833
Venous engorgement	362.37	H34.821 H34.822 H34.823

ICD = International Classification of Diseases; CM = Clinical Modification used in the United States

Additional information for ICD-10 codes:

- For bilateral sites, the final character of the codes in the ICD-10 CM indicates laterality. If no bilateral code is provided and the condition is bilateral, separate codes for both the left and right side should be assigned. Unspecified codes should be used only when there is no other code option available.
- When the diagnosis code specifies laterality, regardless of which digit it is found in (i.e., 4th digit, 5th digit, or 6th digit):
    - Right is always 1
    - Left is always 2
    - Bilateral is always 3

LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in March 2018; the search strategies are provided at www.aao.org/ppp. Specific limited update searches were conducted after June 2019.

(retinal vein occlusion/pathology[majr] OR retinal artery occlusion/pathology[majr] OR retinal vein occlusion/physiology[majr] OR retinal artery occlusion/physiology[majr] OR retinal vein occlusion/physiopathology[majr] OR retinal artery occlusion/physiopathology[majr])

(retinal vein occlusion/surgery[mh] OR retinal artery occlusion/surgery[mh] OR retinal vein occlusion/therapy[mh] OR retinal artery occlusion/therapy[mh] OR retinal vein occlusion/drug therapy[mh] OR retinal artery occlusion/drug therapy[mh])

(retinal vein occlusion/diagnosis[MeSH Major Topic] OR retinal artery occlusion/diagnosis[MeSH Major Topic])

(("retinal vein occlusion"[MeSH Major Topic] OR "retinal vein occlusion"[tiab]) AND (risk[tiab] OR risk factors[mh])) OR Retinal Artery Occlusion/complications[mh]

retinal vein occlusion[majr] AND (quality of life[mh] OR QoL[All Fields])

retinal vein occlusion[majr] AND (Cost-Benefit Analysis[mh] OR Cost of Illness[mh] OR economics[MeSH Terms] OR cost[All Fields] OR cost[MeSH Terms])

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course
Retina and Vitreous (Section 12, 2019–2020)

Focal Points
Retinal Arterial Occlusions (2010)
Update on Retinal Vein Occlusions (2017)

Ophthalmic Technology Assessment –
Published in *Ophthalmology*, which is distributed free to Academy members; links to full text available at www.aao.org/ota.
Therapies for Macular Edema Associated with Central Retinal Vein Occlusion (2015)

Patient Education
Face-Down Recovery After Retinal Surgery Brochure (2014)
Retina Informed Consent Video Collection (2013)
Retinal Vein Occlusion Brochure (2014)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp.
Comprehensive Adult Medical Eye Evaluation (2015)
To order any of these products, except for the free materials, please contact the Academy's Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or www.aao.org/store.

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