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Management of Central Retinal Vein Occlusion

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Abstract:

Central retinal vein occlusion (CRVO) is a major retinal vascular disorder and an important cause of visual impairment, particularly in older adults. Visual loss is mainly related to macular edema, retinal ischemia, and neovascular complications. Management primarily focuses on treating macular edema, monitoring retinal perfusion, preventing neovascular complications, and controlling associated systemic risk factors. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents represent the current first-line therapy for CRVO-related macular edema. Ranibizumab and aflibercept have demonstrated substantial improvements in visual acuity and retinal thickness, while newer treatment options, including aflibercept 8 mg and faricimab, may provide effective disease control with the potential for extended treatment intervals. Intravitreal corticosteroids, including triamcinolone acetonide and dexamethasone implants, remain useful alternatives in selected patients, although their use is limited by the risks of intraocular pressure elevation and cataract progression. Macular grid laser has no established role in CRVO-related macular edema. In ischemic CRVO, close surveillance is essential for early detection of neovascularization, with panretinal photocoagulation indicated after neovascularization develops. Persistent vitreous hemorrhage preventing adequate laser treatment may require pars plana vitrectomy with intraoperative panretinal photocoagulation. Prognosis is strongly influenced by retinal perfusion status, baseline visual acuity, and the severity of macular damage, with ischemic CRVO generally associated with substantially poorer visual outcomes.

Keywords: Central retinal vein occlusion; CRVO; Macular edema; Anti-VEGF; Intravitreal therapy; Aflibercept; Ranibizumab; Faricimab; Dexamethasone implant; Neovascularization.

Introduction:

Retinal vein occlusion (RVO) is a common retinal vascular disorder characterized by obstruction of the retinal venous system by thrombus formation, leading to impaired blood drainage, increased venous pressure, and subsequent retinal ischemia and edema **(1).** RVO represents the second most prevalent retinal vascular disease after diabetic retinopathy and is a major cause of visual impairment worldwide, particularly among older adults **(2).**

RVO is primarily classified according to the site of venous obstruction into central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). CRVO results from occlusion of the main retinal vein, typically posterior to the lamina cribrosa, leading to widespread involvement of all retinal quadrants. In contrast, BRVO occurs at arteriovenous crossings and affects a localized retinal sector. Although BRVO is more common, CRVO is generally associated with more severe retinal ischemia and poorer visual outcomes **(1).**

The management of CRVO aims to preserve vision and prevent sight-threatening complications, with macular edema representing the principal therapeutic target. Intravitreal anti-VEGF therapy is the current first-line treatment and is administered repeatedly according to visual acuity and OCT-guided disease activity. Intravitreal

injection of corticosteroids may be considered in selected patients with an inadequate anti-VEGF response or difficulty maintaining frequent injections, although they carry increased risks of intraocular pressure elevation and cataract progression **(3).**

Early detection and treatment of retinal ischemia and neovascular complications are essential in CRVO. Ischemic eyes require close follow-up during the first months, including slit-lamp examination, gonioscopy when indicated, and fundus evaluation. PRP is recommended once iris, angle, disc, or retinal neovascularization develops, while anti-VEGF therapy may be used as an adjunct **(3,4).**

CRVO management also includes identification and control of associated systemic risk factors, particularly hypertension, diabetes mellitus, hyperlipidemia, cardiovascular disease, sleep apnea, and selected hypercoagulable states. Coordination with the primary care physician or internist is recommended, while broader thrombophilia evaluation may be considered in younger patients and in bilateral, recurrent, or thrombosis-associated cases **(3,5).**

Treatment of macular edema

In CRVO, macular edema is the main cause of visual loss, and intravitreal anti-VEGF therapy is the current first-line treatment, with repeated injections guided by visual acuity and OCT findings. Intravitreal triamcinolone or dexamethasone implant may be considered in eyes with an inadequate anti-VEGF response or difficulty maintaining frequent injections, although these agents carry higher risks of intraocular pressure elevation and cataract progression **(3,6).**

Macular Grid Laser

Macular grid laser photocoagulation has no established role in the treatment of cystoid macular edema secondary to CRVO, as it does not result in significant visual acuity improvement. This was demonstrated by the Central Vein Occlusion Study (CVOS), and current treatment strategies therefore favor pharmacologic intravitreal therapy over macular laser for CRVO-related macular edema **(7).**

Intravitreal Therapy

Intravitreal injection of anti-VEGF agents

Ranibizumab

The phase III CRUISE trial evaluated monthly intravitreal ranibizumab for CRVO-related macular edema in 392 patients randomized to 0.3 mg, 0.5 mg, or sham treatment for six months. At month 6, mean BCVA gains were 12.7 and 14.9 letters in the ranibizumab groups versus 0.8 letters with sham, while 46.2% and 47.7% of treated patients gained at least 15 letters compared with 16.9% in the sham group. Both ranibizumab doses also produced substantial reductions in central foveal thickness. No cases of endophthalmitis, retinal tear, or retinal detachment were reported during the six-month controlled period, establishing ranibizumab as an effective and generally well-tolerated treatment for CRVO-related macular edema **(8).** Ranibizumab 0.5 mg/0.05 mL is approved for macular edema following retinal vein occlusion **(9).**

Aflibercept 2 mg

The phase III COPERNICUS and GALILEO trials established the efficacy and safety of intravitreal aflibercept 2 mg for macular edema secondary to CRVO. In both trials, patients initially received monthly intravitreal aflibercept 2 mg or sham injections. At week 24, gains of at least 15 letters were achieved in 56.1% of aflibercept-treated patients compared with 12.3% in the sham group in COPERNICUS, and in 60.2% compared with 22.1% in GALILEO. Mean BCVA gains were approximately 17–18 letters and were accompanied by marked reductions in central retinal thickness. Treatment was generally well tolerated, with serious ocular adverse events being uncommon. These findings support intravitreal aflibercept 2 mg as an effective treatment for CRVO-related macular edema **(10,11).**

Aflibercept 8 mg

The phase III QUASAR trial randomized 892 patients with macular edema following central, hemiretinal, or branch retinal vein occlusion to aflibercept 8 mg every 8 weeks after 3 or 5 initial monthly doses, or aflibercept 2 mg every 4 weeks. At week 36, both aflibercept 8 mg regimens achieved non-inferior BCVA gains compared with monthly aflibercept 2 mg while requiring fewer injections, with mean injection numbers of 6.1, 6.9, and 8.8, respectively. The safety profile of aflibercept 8 mg was similar to that of aflibercept 2 mg. Based on these findings, EYLEA HD received FDA approval in November 2025 for macular edema following retinal vein occlusion, with dosing every 4 weeks for the first 3–5 doses followed by every 8 weeks, and possible resumption of monthly dosing if the response is not maintained **(13-14).**

Ziv-aflibercept

Intravitreal ziv-aflibercept is a lower-cost, off-label anti-VEGF option that has the same molecular structure and mechanism of action as aflibercept but is formulated and approved for systemic treatment of metastatic colorectal cancer rather than ophthalmic use **(15).**

In a 12-month interventional case series of six treatment-naïve eyes with CRVO-related macular edema, mean visual acuity improved from 0.86 to 0.33 logMAR, while central macular thickness decreased from 519 to 255 μm. No uveitis, cataract progression, intraocular pressure elevation, or systemic adverse events were reported. These findings support the potential efficacy and short-term safety of intravitreal ziv-aflibercept in CRVO, although the small sample size limits the generalizability of the results **(16).**

More recently, Sinawat et al. reported the 6-month interim results of a randomized non-inferiority trial involving 24 treatment-naïve patients with CRVO-related macular edema. Both ziv-aflibercept and bevacizumab produced significant visual and anatomical improvement. Ziv-aflibercept met the non-inferiority criterion for anatomical outcomes, whereas non-inferiority for visual outcomes could not be established. However, no statistically significant differences were observed between the two groups **(17).**

A pooled safety analysis of 5,914 intravitreal ziv-aflibercept injections administered to 1,704 eyes with various retinal disorders found that serious ocular and systemic adverse events were uncommon. These findings support an acceptable overall safety profile for intravitreal ziv-aflibercept, although the analysis was not limited to patients with CRVO **(18).**

Overall, the available evidence supports intravitreal ziv-aflibercept as a promising and economical off-label treatment for CRVO-related macular edema, particularly in resource-limited settings. However, larger CRVO-specific randomized controlled trials are required before it can be considered an alternative to established licensed anti-VEGF agents **(15-18).**

Faricimab

Faricimab is a humanized bispecific monoclonal antibody for intravitreal use that neutralizes both angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A). This dual mechanism is relevant in retinal vein occlusion, as Ang-2 contributes to vascular instability, inflammation, and increased vascular permeability, thereby participating in CRVO-related macular edema **(19).**

The phase III COMINO trial randomized 729 treatment-naïve patients with center-involved macular edema due to CRVO or hemiretinal vein occlusion to faricimab 6 mg or aflibercept 2 mg every 4 weeks through week 24. Faricimab was noninferior to aflibercept for mean BCVA gain (+16.9 vs. +17.3 letters) and produced comparable reductions in central subfield thickness (−461.6 vs. −448.8 μm). Absence of macular leakage was achieved in a greater proportion of faricimab-treated eyes (44.4% vs. 30.0%), with a safety profile comparable to aflibercept **(19).**

In summary, these findings support faricimab as an effective and well-tolerated treatment for macular edema secondary to CRVO or hemiretinal vein occlusion. Faricimab is FDA-approved for macular edema following retinal vein occlusion, and the U.S. label was updated in April 2026 to permit continued individualized treatment beyond 6 months **(20, 21).**

Intravitreal injection of triamcinolone acetonide

The Standard Care Versus Corticosteroid for Retinal Vein Occlusion (SCORE) study evaluated intravitreal triamcinolone acetonide (IVTA) for macular edema secondary to CRVO. A total of 271 patients were randomized to observation, 1 mg IVTA, or 4 mg IVTA. At 12 months, gains of at least 15 letters were achieved in 6.8%, 26.5%, and 25.6% of patients, respectively, with no significant difference between the two IVTA doses or in retinal thickness among the groups. Steroid-related adverse events were more frequent with the 4-mg dose; intraocular pressure-lowering medication was initiated in 8%, 20%, and 35% of the observation, 1-mg, and 4-mg groups, respectively, while new or progressive lens opacity occurred in 18%, 26%, and 33% of phakic eyes. These findings support IVTA as an effective treatment for CRVO-related macular edema and favor the 1-mg dose because it provides similar visual efficacy with a better safety profile than the 4-mg dose **(22).**

Intravitreal injection of dexamethasone implant (Ozurdex)

The GENEVA study evaluated the efficacy and safety of the dexamethasone intravitreal implant (Ozurdex) for macular edema secondary to retinal vein occlusion, including CRVO. A total of 1,267 patients were randomized to receive a 0.7 mg implant, a 0.35 mg implant, or sham treatment. Both implant doses produced faster gains of at least 15 letters and greater reductions in retinal thickness than sham, with the greatest visual benefit observed between days 30 and 90. Intraocular pressure elevation was generally transient and manageable, while cataract rates did not differ significantly during the 6-month follow-up. These findings support the efficacy and acceptable safety of the dexamethasone intravitreal implant for macular edema secondary to retinal vein occlusion **(23).**

Treatment of neovascularization

The Central Vein Occlusion Study (CVOS) demonstrated that prophylactic panretinal photocoagulation (PRP) should not be routinely performed in ischemic CRVO before the development of iris or angle neovascularization, provided that close follow-up is feasible, because early PRP did not completely prevent anterior segment neovascularization and regression after subsequent PRP was more frequent in previously untreated eyes **(24).** Therefore, prompt PRP is recommended once iris or angle neovascularization develops, while intravitreal anti-VEGF therapy may be used as an adjunct. Close follow-up during the early months, including careful iris examination and gonioscopy, is essential for early detection and treatment of neovascularization **(3,25).**

Treatment of Vitreous hemorrhage

Vitreous hemorrhage may cause sudden visual loss and prevent adequate panretinal photocoagulation (PRP) in ischemic CRVO. Persistent or non-clearing hemorrhage may require pars plana vitrectomy with intraoperative PRP. In a retrospective study of 83 eyes, this approach was associated with better final visual acuity and a lower incidence of neovascular glaucoma than no vitrectomy (14.3% vs. 37%). Intravitreal anti-VEGF may be used as an adjunct but should not replace definitive PRP. These findings support vitrectomy with intraoperative PRP when vitreous hemorrhage prevents adequate laser treatment **(3,26).**

Prognosis

Visual prognosis in CRVO is determined mainly by retinal perfusion status, presenting visual acuity, and the severity of macular damage. Nonischemic CRVO generally has a better outcome; final visual acuity of 20/100 or better was reported in 83% of nonischemic eyes compared with only 12% of ischemic eyes **(27).**

Nonischemic CRVO generally has a favorable prognosis, particularly when presenting visual acuity is good and macular edema resolves. Persistent visual impairment is mainly related to foveal pigmentary degeneration, epiretinal membrane formation, or both. Nevertheless, close follow-up is essential because initially perfused eyes may convert to ischemia, with conversion occurring most rapidly during the first 4 months **(27).**

Ischemic CRVO has a poor prognosis because of severe retinal nonperfusion and macular ischemia. Iris neovascularization develops in about 50% of cases, usually within 2–4 months, placing these eyes at high risk of neovascular glaucoma. Therefore, close surveillance during the early months is essential **(3).**

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