Review

SERV clinical practice guidelines: management of retinal vein occlusion


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ABSTRACT

Purpose: A guidelines for the management of retinal vein occlusion is presented. This is necessary because at this moment several therapeutic alternatives have been developed although their role is not yet sufficiently defined.

Methods: Review of the literature for evidence published up to date. Relevant literature was identified and the level of evidence graded. Evidence was then assessed for consistency, applicability and clinical impact. The information was contrasted with those guides published in other countries.

Results: Taking into account the different options of treatment that are currently used, several modes of action are suggested. The role of the various complementary examinations are discussed and it is recommended that criteria for the treatment are based on clinical, angiographic, and tomographic findings.

Conclusions: Although there is no overall consensus, these guidelines promote a good standard of clinical practise and provide an update of the management of retinal vein occlusion.

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Objectives of the guide

The purpose of this guide is to present general guidelines for the classification, diagnostic and treatment of retinal venous occlusions (RVO) at a time in which new therapeutic alternatives are appearing with vaguely defined roles.

This guide suggests lines of action for the different clinical variants but does not aim at establishing criteria of required fulfillment or exempting the ophthalmologist from his/her duty to analyze a specific case and proceed according to the best professional criterion. In addition, it is not intended at all to restrict the freedom of the ophthalmologist in the decision making process for treating a specific patient. Accordingly, the professional may opt for a different prescription within the required usual techniques in the understanding that, according to his or her experience, the desired result calls for a different type of therapy. The fact that such option is not included in this document as a recommended procedure cannot be considered at all as poor professional practice or an infringement of the lex artis ad hoc.

In order to establish said guidelines, a broad review of literature and existing protocols has been carried out by a commission named to this end by the Spanish Retina and Vitreous Society. The various therapeutic options available at present and their most accepted indications have been discussed, so that the clinic, diagnostic and therapeutic recommendations are based on scientific knowledge and levels of evidence.

Said levels of evidence and degrees of recommendation are based on the US Agency for Health Research and Quality:

Evidence Level 1. 1a: The evidence arises from meta-analysis of controlled, randomized and well designed essays. 1b: The evidence arises from at least one, randomized controlled essay

Evidence Level 2. 2a: The evidence arises from at least one controlled, non-randomized and well designed study. 2b: The evidence arises from at least one not completely experimental well designed study such as a cohort study. It refers to a situation in which the application of an intervention is beyond the control of researchers even though its effect can be assessed.

Evidence Level 3. The evidence arises from descriptive, non-experimental, well designed studies such as comparative studies, correlation studies or case and control studies.

Evidence Level 4. The evidence arises from documents or viewpoints of expert committees or clinical experience of renowned authorities or a study of series of cases.


Management of retinal venous occlusions

Anatomic classification

This classification enables the differentiation of entities with different natural history, prognosis and treatment.1-3

1. Central retinal vein occlusion (CRVO): occlusion of the central retinal vein located in the optic nerve.

2. Retinal venous branch occlusion (RVBO):
   - Major or main RVBO: Occlusion of the first order branch exterior to the papilla but involving macular branches.
   - Macular or minor RVBO: involves only one macular branch.
   - Peripheral or secondary RVBO: occlusion of a venous branch, which does not affect macular circulation and is frequently asymptomatic.

3. Hemicentral retinal vein occlusion (HemiC-RVO): occlusion of the main superior or inferior branch of the central
retinal vein at the papillary level, typically included among the branch occlusions. However, its clinical development, prognosis and management is closer to CRVO. When the occlusion occurred outside of the papilla, the occlusion point is visible and, due to the anatomic division arrangement, involves the entire superior or inferior hemi-retina. It is defined as a hemi-retinal occlusion but, in contrast to the Henley central occlusion, it is not virtually identical to the RVBO.

**Physiopathology and risk factors**

The formation of thrombi is the primary physiopathological factor, with endothelial proliferation and inflammatory reactions being secondary effects.  

1. **CRVO**: anatomical factors such as proximity of artery and central vein in the cribiform plate, localization, thinning of vessels in passage, which could lead to the appearance of turbulences and formation of thrombi.

2. **RVBO**: arteriovenous crossing due to the veing being compressed under the artery (Gunn sign) in sclerohypertensive retinopathy. The artery and vein share the same adventitious and their vascular walls are joined.

**Risk factors (table 1)**

Occasionally, retinal vascular occlusions express a systemic process with increased morbidity and mortality.

Typical risk factors: arterial hypertension (AHT) and diabetes.  

1. **Open angle glaucoma**: present in 40% of patients with CRVO (or who will develop it).

2. **AHT**: the most important risk factor, mainly in patients over 60 (association in up to 64% of cases). When AHT is not controlled, it is associated to recurrence of the occlusive condition or the involvement of the other eye.

3. **Diabetes**: probably not due to DM itself but to the associated increase of other cardiovascular risk factors.

4. **Hyperlipidemia** (the main risk factor in patients under 50), is also present in half of the patients over 50.

5. **Blood hyperviscosity** (polycythemia, high levels of fibrinogen, Waldenstrom macroglobulinemia).

6. **Thrombophilia** (greater predisposition to the formation of thrombi), such as antiphospholipid antibodies (anticardiolipin and lupic anticoagulant), hyperhomocisteinemia (risk of vascular disease, concentration-dependent, independent of the rest of factors) and natural anticoagulant system (Leiden factor V, protein C, protein S and antithrombine III).

It is recommended to discard hyperhomocisteinemia in all patients with central retinal vein occlusion; levels exceeding 11µmol/l increase the risk of atherosclerotic disease in asymptomatic individuals. The recommended levels are in the range of 9-10µmol/l by means of vitamin complexes containing folic acid.

The antiphospholipid syndrome (APS) is characterized by increased hypercoagulability with repetition thrombosis (arterial and venous), morbidity in pregnancy (recurring fetal abortion) and blood alterations (thrombopenia and/or hemolitic anemia). The best known are the lupic anticoagulant and anticardiolipine antibodies. 29% of patients with primary APS exhibit ocular alterations such as vascular tortuosity, cotton-like exudates and small occlusions detectable by means of fluorescein angiography (FAG).

Hormone substitution therapy and oral contraceptives: greater risk of venous occlusion. Not to be established in women with a history of retinal thromboembolic events. Discontinuing this treatment after a thrombosis is controversial (it is usually discontinued, although it must be assessed on an individual basis for each case).

Other infrequent processes: Retinal vasculitis, Behçet disease, nodular polyarthrititis, Wegener granulomatosis.

**Role of the ophthalmologist in the study of systemic risk factors**

Retinal vascular occlusions are associated to a higher risk of death due to heart or brain vascular events. It is the responsibility of the ophthalmologist to study the mean systemic risk factors, interpret results and refer to the adequate specialist. As a general rule, medical management of risk factors must be initiated within two months after diagnostic.

Patient under 50 years of age usually exhibit risk factors such as AHT or hyperlipidemia, but on some occasions it is impossible to find an underlying cause.

Table 2 illustrates a protocol for requesting analysis in RVO.

**Clinical expressions**

**Central retinal vein occlusion**

**Symptoms**: sudden, severe and painless visual loss (more acute in ischemic forms). Extensive loss of visual field.

**Signs**: acute phase: venous tortuosity and dilatation, superficial hemorrhages, macular edema (ME), papilla edema and peri-papillary cotton-like exudates in the four quadrants of the retina. Afferent pupil defect (ischemic forms). **Chronic phase**: call lateral vessels in papilla and retina, persistent venous dilatation and tortuosity, venous sheathing, arteriole narrowing and macular anomalies (chronic ME macular pigmented alterations). Neovascularization (15-34% non-ischemic forms; 50% ischemic forms).

**Retinal venous branch occlusion**

**Symptoms**: sudden moderate visual loss (if the macula is involved). ME is the most common cause of chronic visual loss. Sectoral/altitudinal campimetric scotoma or loss (the latter only in ischemic forms).

**Signs**: acute phase: venous dilatation and superficial retinal hemorrhage in a well-defined sector (venous drainage area). Other signs: ME, cotton like exudates, arteriole narrowing. **Chronic phase**: collateral vessels, microaneurisms, chronic macular alterations: persistent ME, alteration of the retina pigmented epithelium (RPE), subretinal fibrosis, epiretinal membranes. Papillary neovascularization (PNV) or retinal neovascularization (NVR) (36% of cases are ischemic forms), vitreous hemorrhage.
**Hemicentral retinal vein occlusion**

**Symptoms:** sudden visual loss with typically altitudinal campimetric defect (in ischemic forms).

**Signs:** venous dilatation and retinal hemorrhages involving the superior or inferior hemi-retina, equally affecting the nasal and temporal quadrant. Additional signs of venous occlusion. From a clinical and physiopathological viewpoint, it is closer to central vein occlusion, although with higher neovascularization risk.16

**Supplementary tests**

**Fluorescein angiography (FAG)**

FAG distinguishes between ischemic and non-ischemic venous occlusions. It determines the extension of the ischemia and the ME, in addition to confirming a diagnostic in doubtful cases and differentiates between telangiectasias and neovessels. It could have prognostic value in recovering visual acuity (VA), in assessing the macula and the presence of severe macular ischemia with enlargement of the avascular foveal area, particularly in the ischemic forms of CRVO. Generally, FAG is not performed in the acute phase of RVO due to the screen effect of hemorrhages. The usual practice is to wait between 3 and 6 months from the acute phase.

**Central retinal vein occlusion**

Differentiates ischemic and non-ischemic forms (retinal ischemia is defined by the presence of 10 or more disc areas (DA) without retinal perfusion).17

**Signs in FAG:** delay in arterial-venous circulation (higher in ischemic forms), hypofluorescence due to screen effect, non-perfusion areas (ischemic forms), staining and venous wall exudation, macular oozing in late phases. In chronic phases: collateral and/or neovessels.

1. **Non-ischemic, partial, edematous or hyperpermeable CRVO:** 75% of cases. Best prognosis; the major complication is cystoid ME. A third can evolve to ischemic forms18 (fig. 1).

2. **Ischemic or total CRVO:** 25% of cases. Worst prognosis. Neovessels are developed in 35% of cases.19 The main complication is neovascular glaucoma: the risk of neovessels in iris is higher if the retinal ischemia area exceeds 10 AD20 (fig. 2).

**Retinal venous branch occlusion**

It allows for differentiating non-ischemic RVBO from ischemic RVBO: higher neovascularization risk (36% is the ischemic area > 5 DA).21

**Signs in FAG:** delay in venous filling, hypofluorescence due to screen effect (hemorrhage), hypofluorescence due to no capillary perfusion (ischemia), diffuse hyperfluorescence in late phases (oozing, edema), increased permeability and venous wall staining. (figs. 3 and 4)

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**Figure 1 – Edematous CRVO.**

**Figure 2 – Ischemic CRVO.**
Hemicentral retinal vein occlusion

It enables distinguishing non-ischemic (78% of cases)\textsuperscript{22} from ischemic forms.

Signs in FAG: as described for RVBO, affecting both quadrants (hemiretina).

**Optic Coherence Tomography (OCT)**

This technology is essential for studying venous occlusions in order to evaluate quantitatively and qualitatively the existence of ME and the response to treatment.

OCT must be carried out:

1. At diagnostic time and before treatment (the indication and the type of treatment largely depend on the OCT results).

Follow-up visits after treatment must be monthly or quarterly during the first year. If the patient remained stable in the second year, follow-up visits can be every six months and then once a year.

**Diagnostic**

1. Characterization of the ME: it provides quantitative information (retinal thickness measurement) and qualitative information (morphological changes associated to the accumulation of liquid).
2. Study of the vitreo-macular interphase.

Morphological changes:

1. Retinal thickening with or without cystic spaces (single, multiple cyst or coalescence) (fig. 5).
2. Increased reflectiveness with screen effect in case of hemorrhage.
3. Alteration of the foveal depression.
4. Neurosensory retinal detachment (NSRD) with sub retinal liquid (most frequent in ME caused by venous occlusion is then in other conditions, due to the retinal pigmentary epithelium damage (RPE) secondary to inflammation and ischemia and the increase of intra-retinal fluid).\textsuperscript{23} It explained the poor vision of the patient (fig. 7).
5. Presence of epiretinal membrane (ERM) or macular hole (MH)\textsuperscript{24} (fig. 6).
6. Assists in localizing the thickened areas in order to guide the laser treatment with FAG.

**Treatment**

1. Follow up of patients through retinal thickness variations (quantitative assessment of the therapeutic response).
2. Follow up sequential evaluation: improvement or worsening of ME (indication for re-treatment with VA changes).
3. Assessment of associated complications (lamellar holes after rupture of a cyst, formation on ERM, complete AM, vitreo-macular traction syndrome).

Figure 8 illustrates the contribution of the ocular fundus study, FAG and OCT.

**Ophthalmological treatment of retinal venous occlusions**

The treatment objectives are to act upon the ophthalmological complications which cause visual acuity reduction and threaten total or partial loss of vision, as well as the identification and action on modifiable systemic factors.

Figure 5 – Formation of large cystic spaces.

Figure 6 – Presence of epiretinal membrane in patient with central vein occlusion.

Figure 7 – Foveal detachment in patient with retinal venous occlusion.
Treatment of retina central vein occlusions (fig. 9)

As commented above, associated systemic diseases must always be treated. There is no evidence that early treatment on the ocular globe will modify the visual prognosis in established CRVO cases.

The main problem is to differentiate between ischemic and non-ischemic forms. Evidence Level 3. Recommendation degree C.

Ischemic retina central vein occlusion

Follow up: Monthly checkups to discard iridian neovascularization (INV) or angle neovascularization (ANV). It could be enough to check up every 2-3 months unless specific risk factors exist. Evidence Level 1. Recommendation degree A.

PFC when the first sign of INV or NVA appears. Evidence Level 1. Recommendation degree A.

Prophylactic PFC when prescribed controls cannot be carried out. Evidence Level 3. Recommendation degree C.

In 90% of cases, the regression of INV/ANV occurs between one and two months after PFC. The persistence of neovessels must be controlled and a supplementary PFC can be carried out.

The presence of PNV or NVR without INV/ANV must be treated with PFC in order to prevent neovascularization of the anterior segment.

The protective effect of intravitreal triamcinolone acetonide (IVTA) on anterior neovascularization is not proved. Evidence Level 4. Recommendation degree D.

Non-ischemic retina central vein occlusion

Regular checkups for three years to detect conversion to ischemic retina due to the greater risk of progression during this period of time. The prognosis is reasonably positive if there is no evolution towards the ischemic form, with a restoration of VA of about 50% (the main cause of poor VA is chronic cystoid ME). The prognosis depends on the initial VA.

Follow-up: VA of 20/40 or above: control every 1-2 months during 6 months and then annually if the process is stable. VA under 20/200: monthly control for the first six months and every two months for the following six months (higher degree of lack of perfusion and risk of developing INV/ANV). VA between 20/50 and 20/200: monthly checkup during the first six months (medium risk of developing INV/ANV).

If at any time VA falls below 20/200, it will be necessary to make an evaluation of the perfusion condition with monthly follow-up for a further six months.

Treatment of neovascular glaucoma

Retinal panphotocoagulation (PFC) can be beneficial for treating neovascular glaucoma. Evidence Level 3. Recommendation degree C.

If the eye is amaurotic, the objective is to maintain it painless, usually with topical steroids and atropine.

If the eye has vision, intra-ocular pressure is controlled with anti-glaucomatous drugs or cycloablative procedures.

If the eye has vision, intra-ocular pressure is controlled with anti-glaucomatous drugs or cycloablative procedures. Evidence Level 4. Recommendation degree D.

The utilization of intravitreal or intra-chamber bevacizumab produces a regression of INV and NVA. The iris neovessels regress faster when bevacizumab is utilized in combination with PFC than when utilizing only PFC. Bevacizumab can reduce the need of carrying out surgery and can serve as adjuvant in filtrating surgery.

Treatment of macular edema (fig. 10)

There is no effective treatment for ME associated to CRVO.
Grid photocoagulation does not produce any benefit and is not recommendable. The Central Vein Occlusion Study did not observe significant differences in VA between treated with grid laser and untreated eyes. Evidence Level 1. Recommendation degree A.

Treatment with IVTA can achieve a temporary improvement at the anatomic and functional level of ME associated to CRVO (studies of series of cases) requiring multiple injections to sustain the effect. Many patients do not experience VA improvements. The optimum dose is not clear, although the most widely used dose is 4mg. Evidence Level 4. Recommendation degree D.

The long-term safety and efficacy of IVTA is being researched in a multicentre clinical trial, the SCORE study (Standard Care versus Corticosteroid for Retinal Vein Occlusion Study), which compares the efficacy and safety of 1mg and 4mg dosages of intravitreal triamcinolone without preservatives against observation in eyes with loss of vision associated to ME secondary to a non-ischemic CRVO. The results published to date conclude that the use of intra-victory triamcinolone is superior to observation, and that the dose of 1mg has a safety profile superior to that of the 4mg dose. Evidence Level 1. Recommendation degree A.

In addition, a multicentre randomized clinical trial has assessed the results of intravitreal dexamethasone implants (Ozurdex®). The GENEVA Study - Global evaluation of implantable dexamethasone in retinal vein occlusion with macular edema- spanned 6 months and was expanded to cover 12 months to analyze the efficacy and safety of 350µg and 750µg of Ozurdex® in OVR. In the CRVO cases, the drug was well tolerated, exhibiting a significant improvement of VA with both dosages at 30, 60 and 90 days. However, the improvement was not significant at 180 days. The macular thickness changes identified with OCT were significant at the 90 days of the study and ceased to be significant at 180 days. Evidence Level 1. Recommendation degree A.

In various series of cases, it was stated that treatment with intravitreal anti-angiogenic drugs (anti-VEGF) could diminish macular thickness, reduce retinal hemorrhages and improve visual acuity. However, the follow up periods of these series are short. At present, this treatment cannot be recommended. Evidence Level 4. Recommendation degree D.

Similarly, several publications suggest that the intravitreal administration of bevacizumab in the initial period of non-ischemic CRVO could reverse ME and retinal hemorrhages and improve vision. However, as in said initial stages of the disease spontaneous resolution can occur as part of its natural history, this treatment cannot be recommended on the basis of the current evidence. Evidence Level 4. Recommendation degree D.

The results of the CRUISE Study are expected to be published in 2010. CRUISE is a clinical trial that assesses the efficiency of ranibizumab for treating macular edema secondary to CRVO. The preliminary results of this study revealed an increased vision of patients after a six month follow up. Evidence Level 1. Recommendation degree A.

Figure 9 – CRVO management algorithm.
Experimental treatments
Laser-induced chorioretinal anastomosis is an experimental treatment that has not yet clearly demonstrated benefits. In addition, various complications associated to this procedure have been described, including choroidal neovascularization, retinal and subretinal traction and fibrosis and hemovitreous.

Treatment of retinal venous branch occlusions (fig. 12)
As in CRVO, associated systemic diseases must always be treated.
ME and NVR or PNV are the two main complications of RVBO which can be treated.
Neovascularization takes place in 36% of eyes with non-perfusion areas > 5 DP and in 62% of eyes with > 10 DP.
Treatment of neovascularization
Neovascularization occurs only with the closure of papillaries of at least one quadrant and generally takes place within six months after the occlusion.
NVR and PNV are an indication for performing photocoagulation in the ischemic retina area (sectoral photocoagulation). Evidence Level 1. Recommendation degree A.
The photocoagulation must be carried out once the neovascularization has occurred but not as a prophylactic measure.
Follow-up: every 3-4 months in patients exhibiting ischemia in one or more quadrants (fig. 13).

Treatment of macular edema
Grid laser in the capillary diffusion area can be beneficial after a period of 3 to 6 months from the onset of the disease and when most of the hemorrhagic component has been reabsorbed. Evidence Level 1. Recommendation degree A (fig. 14).
If the vision is reduced to 20/40 or worse, three to six months must elapse before the hemorrhagic component has reabsorbed. Grid macular photocoagulation is recommended when the vision loss is of 20/40 or worse without improvement and is due to ME with a good macular perfusion. However, if the ME is due to a...
lack of macular perfusion, said laser treatment is not recommended.55

Checkups: The first must be three months after the occlusion and subsequently at 3-6 month intervals depending on the possible complications and their treatment or lack thereof.

Prognosis: Between one third and a half of patients with RVBO recover their eyesight to 20/40 or better without treatment. Patients with diminished vision secondary to ME exceeding one year have greatly reduced probabilities of recovering their eyesight (figs. 10 and 14).

Intravitreal corticoid injections. IVTA improves vision and reduces ME secondary to ORVR.57-59 Evidence Level 4. Recommendation degree D.

Complications: increase of intra-ocular pressure and formation of cataracts. The long-term safety and efficacy of IVTA is being researched in said SCORE study38,60 (efficacy and safety of 1mg and 4mg doses of preservative-free intravitreal triamcinolone against standard treatment -grid photocoagulation - in eyes with loss of vision associated to ME secondary to RVBO). No VA differences appeared at month 12 but the rate of adverse events (increased intraocular pressure and cataracts) was higher in the 4mg group. According to the study, grid photocoagulation remains as the standard treatment for patients with loss of vision associated to ME secondary to RVBO. Evidence Level 1. Recommendation degree A.

Intravitreous dexamethasone implants (Ozurdex®) has been assessed in the GENEVA study.40 The drug was well tolerated and patients exhibited a significant improvement of the VA at day 30, 60 and 90, which disappeared after 180 days from the treatment. Changes in macular thickness determined with OCT were significant at day 90 of the study and ceased to be significant at 180 days. Evidence Level 1. Recommendation degree A.

Periocular injections of triamcinolone acetonide61,62 exhibit highly reduced efficacy than when the drug is administered intraocularly.62 Evidence Level 3. Recommendation degree C.

Injections of anti-angiogenic drugs:45,63-66 Bevacizumab: evidence based on series of cases with very little follow-up. Multiple injections are required to sustain the effect. The most common treatment pattern is two or three injections in the first 5-6 months.45,63 The authors of this guide recommend a charging phase consisting in a monthly injection for three months, assessing subsequently the need for more injections. Evidence Level 3. Recommendation degree C.

Controlled and randomized studies are needed for a long-term assessment of the efficacy and safety of intravitreal bevacizumab injections. At present, a recommendation
cannot be made for the use of bevacizumab. Evidence Level 3. Recommendation degree C.

Ranibizumab: the preliminary results of the BRAVO essay67 reveal a statistically significant gain in vision of patients after a six month follow up. Evidence Level 1. Recommendation degree A (figs 15 and 16).

Treatment of retinal vein hemicentral occlusion

Similar to the description of RVBO with two exceptions:
1. The risk of rubeosis is higher in ischemic hemicentral venous occlusion than in RVBO but lower than in OVC R.68
2. The risk of PNV is higher in HemiC-RVO than in ischemic CRVO or in ORVR.16

Surgical treatment of retinal venous occlusions

Central retinal vein occlusion

Radial Optic Neurotomy (RON)

Principle: RON is based on the concept of “neurovascular compartmental syndrome”.

Objective: to decompress the external scleral compartment (scleral space, cribriform plate, optic nerve, retina artery and central vein)69,70.

Procedure: pars plana vitrectomy, posterior hyaloid extraction, single radial incision in the nasal side of the papilla to the centre of the cribriform plate, after a FAG to determine the area that is free of large vessels. Evidence Level 3. Recommendation degree C.71

The VA improvement after RON is believed to be due to a faster resolution of ME in CRVO which stimulates the formation of collateral vascularization (optical-ciliary) and the ensuing blood flow improvement.72 There is no evidence supporting the mechanism of increase of retinal vascular flow.72

The anatomic and visual results of RON in various series70-73 seemed to be better in the long term74,75 than the natural history of the disease.19

The combined therapy of RON with intravitreal triamcinolone71,72,76 does not seem to exhibit statistically significant differences with RON on its own.

Potential complications: intra-surgery hemorrhage, laceration of the retina, central vein or artery, ocular globe perforation, retina detachment, visual field defects.
Vitrectomy with or without internal limiting membrane (ILM) peeling
Principle: the mechanism of action is unknown, although hypothetically the improvement is due to an increased oxygen supply to the ischemic retina.77 Another theory sustains that vitrectomy releases the traction of the retinal surface.78,79 In what concerns the internal limiting membrane peeling, the traction derived from the vitreous fibers on the Müller cells increases the risk of cystic ME.80 Evidence Level 3. Recommendation degree C.

Retinal venous branch occlusion

Adventitiotomy of the arterial-venous crossing
Principle: it is believed that RVBO occurs in the arterial-venous crossing, where the artery and vein share a common adventitia;81 AHT and atherosclerosis compressing the vein which gives rise to turbulences, vascular endothelium damage and the formation of a thrombus at the secondary level. Evidence Level 3. Recommendation degree C.

The mechanism of action is to decompress the arterial-venous crossing.82

Procedure: pars plana vitrectomy, posterior hyaloid detachment around the optic nerve and the posterior retina, incision in internal retina to about 100 to 500µm of the arterial-venous crossing which extends parallel to the retinal arteriole to reach the common adventitia, at which point the vessels separate.83,84

The success of adventitiotomy can be partially attributed to the vitrectomy that is performed at the same time.85,86

Potential complications: cataracts, nervous fiber layer defects, hemorrhage, retinal tears, retinal detachment, post surgery glyosis. This is a difficult procedure to perform. The section of the adventitia requires bimanual surgery.

There is no large, randomized and controlled study defending the use of adventitiotomy for the treatment of ME secondary to RVBO, although it is a procedure to be considered particularly in cases with short evolution.

Local anticoagulation

Objective: the utilization of anticoagulants and platelet antiaggregants in order to dissolve the thrombus at the level of the cribiform plate prevent new thrombi to restore the blood flow and improve VA.87,88 Systemic RTPA has been utilized,88 as well as intravitreal RTPA87,89 or by means of catheterization of the ophthalmic artery with urokinase.90 Evidence Level 3. Recommendation degree C.

The effect of RTPA is greater in immature thrombi, but less effective in mature, long evolving thrombi as is the case of OVCR.91

Anticoagulant treatment such as aspirin, heparin or intravenous thrombolytic have not demonstrated sufficient efficacy.

Medical treatment of retinal venous occlusions

As discussed above, it is the responsibility of the ophthalmologist to study the mean systemic risk factors when diagnosing RVO (table 1), request the appropriate analysis (table 2), interpret their results and refer the patient to the specialist to begin treatment if necessary with the objective of preventing associated systemic damages and the recurrence of another venous occlusion, particularly in the second eye.

Anticoagulants and heparin have not proven their efficacy, as well as fibrinolitic agents such as streptokinase or tissue plasminogen activator. Even though it would appear that antiagregant drugs such as aspirin or prostacyclines should have beneficial effects, these could not be demonstrated with evidence level 3. The same can be said of hemodilution.

It has been proven that RVO are associated to an increase of vascular causes of heart and brain death.92 Accordingly, it

<table>
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<th>Table 1 – Risk factors for retinal venous occlusions and scientific evidence level</th>
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<td>Open angle glaucoma</td>
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<tr>
<td>Arterial hypertension</td>
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<td>Diabetes mellitus</td>
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<td>Blood hyperviscosity</td>
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<td>Hyperlipidemia</td>
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<td>Thrombophilia</td>
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is important to use anti-hypertensive drugs for controlling arterial pressure in RVO patients who exhibit AHT as basal disease, as well as the use of statins if necessary, and following the indications of the European guides for controlling and treating AHT.

The recurrence of RVO in the affected eye or its appearance in the other eye can occur in up to 15% of patients. For this reason it is crucial to control the underlying cardiovascular risk factors to reduce this percentage, with a recommendation degree of C.22

For patients under 50, CRVO is generally more benign in a higher number of cases although 15-20% develop important loss of vision and neovascular complications. Even though it has been indicated that systemic corticoid therapy could improve the prognosis of this group, there is no scientific evidence to recommend it. The contraception pill is a frequent antecedent and should be contraindicated in these patients. In addition, inflammatory diseases should be identified, referring the patient to specialists. This age group with RVBO usually exhibits AHT and/or hyperlipidemia as the most frequent underlying systemic disease, which must be treated adequately.

REFERENCES

2. Scott IU, Blodi BA, Ip MS, Vanveldhuisen PC, Oden NL, Chan CK, et al., Score Study Investigator Group. Score Study report

Table 2 – Analyses protocol in vascular occlusions

<table>
<thead>
<tr>
<th>In all patients</th>
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<tbody>
<tr>
<td>Complete hemogram</td>
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<tr>
<td>Sedimentation rate</td>
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<tr>
<td>Prothrombine time</td>
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<td>TTPA</td>
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<td>Fibrinogen</td>
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<td>Lipid profile (cholesterol, VDL, HDL, triglycerides)</td>
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<td>Reactive Protein C</td>
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<td>Urea, electrolytes, creatinin</td>
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In the absence of these risk factors, in patients under 50 years or in bilateral cases:

| Homocistein in plasma |
| Antiphospholipid profile (lupic anticoagulant, antocardiolypin antibody, anti-β2-glycoprotein) |
| Antithrombine III |
| Functional Protein C |
| Functional Protein S |
| Activated resistance protein C (if pathologically, confirm with genetic tests) |
| Leiden Factor V |
| Prothrombine mutation |

If a specific systemic disease is suspected:

| Angiotensin converter enzyme and thorax X-ray (sarcoildosis) |
| Autoantibodies (anti DNA, ANA, ANCA,...) for collagenopathies and vasculitis |
| HLA (Behçet disease) |

22. Hayreh SS, Zimmerman MB, Podhajsky P. Incidence of various types of retinal vein occlusion and their recurrence and


34. The Standard Care vs. COrticosteroid for REtinal Vein Occlusion (SCORE) Study. Clinicaltrials.gov Identifier NCT00105027.


