Review Article

Surgical treatment of central retinal vein occlusion

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ABSTRACT.

The treatment of central retinal vein occlusion (CRVO) is still a subject of debate. Medical therapy efforts, as well as retinal laser photocoagulation, have mostly dealt with management of the sequelae of CRVO, and have shown limited success in improving visual acuity. The unsatisfactory results of such therapeutic efforts led to the development of new treatment strategies focused on the surgical treatment of the occluded retinal vein. The purpose of this review is to summarize the outcomes of commonly reported surgical treatment strategies and to review different opinions on the various surgical approaches to the treatment of CRVO.

Key words: central retinal vein occlusion – surgical treatment – radial optic neurotomy – chorioretinal venous anastomosis – tissue plasminogen activator – retinal vein cannulation

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Introduction

Central retinal vein occlusion (CRVO) is a frequent retinal vascular disorder that causes visual loss in patients during the fifth through seventh decades of life. To date, there is no proven effective treatment for the disorder, despite its frequency and well known clinical appearance (Central Vein Occlusion Study Group 1993; Sharma & D'Amico 2004; Shahid et al. 2006).

The characteristic retinal findings of CRVO include four-quadrant intraretinal haemorrhages, venous tortuosity, a swollen optic disc, retinal and macular oedema and capillary non-perfusion. Central retinal vein occlusion is classified as either ischaemic (non-perfused) or non-ischaemic (perfused), according to clinical and fluorescein angiographic (FA) features of severity. The features that are indicative of an ischaemic CRVO include an initial visual acuity (VA) of ≤ 20/200, the presence of multiple cottonwool spots, an afferent pupillary defect, and ≥ 10 disc areas of capillary non-perfusion on FA (Central Vein Occlusion Study Group 1993; Baumal & Brown 1997). The cases in which excessive retinal haemorrhages prevent accurate visualization of the areas with capillary non-perfusion are categorized as indeterminate CRVO (Central Vein Occlusion Study Group 1993). Among patients with CRVO, 34% develop extensive capillary non-perfusion and retinal ischaemia (Patelli et al. 2004). Almost 30% of the primarily non-ischaemic cases become ischaemic within 4–6 months after first diagnosis (Binder et al. 2007). Ischaemic CRVO has an extremely poor visual prognosis, whereas the non-ischaemic type is usually benign and self-limiting (Hayreh 1983, 2003; Quinlan et al. 1990; Central Vein Occlusion Study Group 1993). The final VA after CRVO depends on the VA at presentation. In the natural history of CRVO, patients with an initial VA of ≤ 0.1 (20/200) Snellen lines have an 80% chance that vision will remain at that level or will worsen over time, whether the CRVO is ischaemic or non-ischaemic (Central Vein Occlusion Study Group 1993, 1997). Iris neovascularization and neovascular glaucoma are frequent complications of CRVO and develop in 40–85% of eyes affected by ischaemic CRVO, but in only 5% of non-ischaemic eyes (Rath et al. 1992; Central Vein Occlusion Study Group 1993; Eye Disease Case–Control Study Group 1996). Electroretinography (ERG) is suggested to be a useful method of predicting the risk of ocular neovascularization in CRVO. In a recent study by Kjeka et al. (2007), photopic 30-Hz flicker ERG with cone b-wave implicit time > 35 milliseconds was reported to be clearly associated with the development of neovascular complications in eyes with CRVO.

Pathogenesis of central retinal vein occlusion

The exact underlying pathogenesis of CRVO remains unknown. It is thought to be a compartment syndrome,

where thrombotic occlusion develops as a result of several local and systemic factors, including compression of the vein by the sclerotic central retinal artery (CRA) in the scleral ring, glaucoma, systemic hypertension, hypercholesterolaemia, diabetes mellitus and hyperviscosity states. The Eye Disease Case–Control Study Group (1996) identified systemic hypertension, chronic open-angle glaucoma and diabetes mellitus as risk factors in approximately 75% of cases of CRVO. Hereditary alterations in the coagulation pathways may also increase the risk for CRVO (Hvarfner et al. 2003; Gumus et al. 2006). Activated protein C resistance, which is caused by a point mutation in factor V (factor V Leiden) is the most common genetic cause of venous thrombosis. The presence of factor V Leiden leads to delayed recirculation and ischaemia, resulting in a higher risk for neovascular complications in CRVO (Hvarfner et al. 2003). Deficiencies of anticoagulant proteins, such as antithrombin III, protein C and protein S, and high levels of activated factor VII, lipoprotein (a), factor VIII, endothelial protein C receptor and hyperhomocysteinaemia have also been reported as other possible risk factors for patients with retinal vein occlusion (Hansen et al. 2000; Gumus et al. 2006). Together, these factors cause a decrease in the venous lumen, leading to increased turbulence and endothelium cell damage with subsequent thrombus formation (Eye Disease Case–Control Study Group 1996; Williamson 1997; Patelli et al. 2004; Poulson et al. 2004; Sharma & D'Amico 2004; Martinez-Jardon et al. 2005; Shahid et al. 2006; Mohamed et al. 2007). This has been supported by histological studies that localized the thrombus in the lamina cribrosa in most cases (Green et al. 1981).

Treatment of central retinal vein occlusion

There is no proven effective treatment for CRVO to date. Previous treatment strategies have mostly aimed to manage the sequelae of CRVO with non-surgical techniques, including retinal laser photocoagulation and medical treatments. However, such treatments neither improve VA, nor effectively decrease retinal haemorrhage and oedema (Elman 1996; Williamson 1997; Lahey et al. 1999; Opremcak et al. 2001; Hayreh 2003).

Medical treatments which aim to instigate thrombolysis and restore venous outflow by the systemic or intravitreal administration of recombinant tissue plasminogen activator (t-PA) have shown only limited success as a result of serious complications, including vitreous and cerebral haemorrhages (Elman 1996; Lahey et al. 1999). As abnormalities of blood and plasma viscosity are often present in patients with CRVO, the reduction of blood viscosity by isovolaemic haemodilution therapy has been widely recommended by the members of the German Retina Society (Höh et al. 2007). However, this treatment has been shown to have limited effect only when started within the first 2 weeks of the onset of CRVO (Hansen et al. 1985, 1989). Moreover, patients with systemic diseases, such as congestive heart failure, respiratory distress or renal insufficiency, should be excluded from such therapies (Glacet-Bernard et al. 2001).

The development of macular oedema is one of the most common findings in CRVO and is the main cause of impaired vision. Reduced blood flow and impaired microcirculation damage the endothelium of the blood–retinal barrier and thus cause increased permeability and plasma exudation into the macula. Moreover, hypoxia-induced expression of vascular endothelial growth factor (VEGF) and other inflammatory mediators trigger the formation of macular oedema (Aiello et al. 1994; Vinores et al. 1997; Stahl et al. 2007). In recent years, intravitreal steroid and certain anti-VEGF antibody injections have been suggested to be beneficial in reversing visual loss caused by macular oedema. Their beneficial effects are attributed to their antiangiogenic and anti-inflammatory effects, which reduce the permeability of endothelial cells and stabilize the blood–retinal barrier (Greenberg et al. 2002; Ip & Kumar 2002; Blumenkranz 2005; Krepler et al. 2005; Iturralde et al. 2006; Stahl et al. 2007). Intravitreal triamcinolone acetonide (IVTA) may be a therapeutic option in the treatment of macular oedema in CRVO, but its potential benefit has to be weighed against the risk of its causing ocular side-effects, such as intraocular pressure (IOP) rise, endophthalmitis and cataract formation. An IOP rise is a significant complication of IVTA injection, may be long-lasting and usually requires treatment with topical antiglaucomatous agents. Gelston et al. (2006) reported a significant increase in IOP within 2 months of IVTA injection, but observed no significant visual improvement in CRVO patients with macular oedema. By contrast with intravitreal steroids, anti-VEGF agents do not cause IOP to rise (Stahl et al. 2007). In a prospective interventional case series including 21 eyes with CRVO (14 eyes) or branch retinal vein occlusion (BRVO) (seven eyes), Stahl et al. (2007) evaluated the course of VA and central retinal thickness after a single bevacizumab injection. They observed a visual improvement ≥ 1 line in all eyes and ≥ 3 lines in 47.6% of eyes within 9 weeks of the injection. They observed no intraocular complications in their patients. However, the effectiveness of this therapeutic approach needs to be proven with prospective clinical studies.

The unsatisfactory results of medical therapy techniques led to the development of novel treatment strategies which focus on the surgical treatment of the occluded retinal vein.

Surgical treatment strategies for central retinal vein occlusion

Common surgical approaches to CRVO can be summarized as follows:

(1) radial optic neurotomy (RON);
(2) chorioretinal venous anastomosis;
(3) vitrectomy with or without internal limiting membrane (ILM) peeling, and
(4) direct injection of t-PA into the lumen of a retinal vein via retinal vein cannulation.

Radial optic neurotomy

Surgical decompression of the central retinal vein (CRV) with RON is a relatively new procedure in the management of CRVO. The benefits and safety of RON are questionable. Some authors describe it as a safe and effective way of protecting VA, but others believe that it is far from being safe,

and does not serve its purpose of decompression of the scleral outlet (Opremcak et al. 2001, 2006a, 2006b; Friedman 2003; Garcia-Arumi et al. 2003; Hayreh 2003; Weizer et al. 2003; Martinez-Jardon et al. 2005; Hasselbach et al. 2007).

Radial optic neurotomy was first described by Opremcak et al. (2001). The authors performed surgical decompression of the vein by making a radial incision of the optic nerve head (ONH), a procedure they designated radial optic neurotomy. They hypothesized that the anatomy of the ONH and scleral outlet might play a role in the development of CRVO (Opremcak et al. 2001). The scleral outlet is defined as the space confined by the scleral ring containing the cribriform plate (lamina cribrosa), CRA, CRV and optic nerve. Increased pressure within the confined scleral outlet was hypothesized to compress the lumen of the CRV and cause thrombus at this location as a result of decreased lumen size and increased turbulence. Release of this pressure via RON would increase the CRV lumen size and venous blood outflow, and thus allow for the clearing of any venous thrombosis. Moreover, RON was thought to induce the postoperative development of optociliary venous anastomosis or retinochoroidal shunts, leading to increased retinal venous outflow (Opremcak et al. 2001; Azad & Verma 2003; Friedman 2003; Garcia-Arumi et al. 2003; Williamson et al. 2003; Nomoto et al. 2004; Spaide et al. 2004; Martinez-Jardon et al. 2005; Hasselbach et al. 2007).

Based on this hypothesis, Opremcak et al. (2001) performed RON to decompress the scleral outlet. They describe the technique as involving an incision on the nasal side of the optic nerve, radial to the nerve and parallel to the nerve fibre layer. Major retinal vessels were avoided during this procedure. The cribriform plate, scleral rim and adjacent sclera were incised and the scleral outlet relaxed. In their pilot study of 11 patients with severe, haemorrhagic CRVO with VA $\leq$ 20/400, Opremcak et al. (2001) reported that RON led to dramatic and rapid clearing of intraretinal haemorrhage and improved retinal blood flow in all patients. Visual acuity improved in 73% of patients, with an average gain of 5 lines of vision, and 64% achieved a final VA $\geq$ 20/200 (Opremcak et al. 2001).

The results reported by Opremcak et al. (2001) were challenged by Hayreh (2003), who opposed findings in favour of RON and suggested that RON was not a safe procedure given the close proximity of the incision site to the CRA. Hayreh (2003) proposed that radial incision of the circle of Zinn and Haller cut off the blood supply to the ONH, resulting in acute ischaemia of the ONH and visual loss, which made the procedure potentially harmful. Hayreh (2003) also proposed that surgical decompression of the vein could not be achieved by RON, as the lamina cribrosa is composed of rigid collagen tissue which will not relax with radial incision at one place. Moreover, Hayreh (2003) suggested that it was unlikely to recanalize the CRV, which was completely obliterated by an organized thrombus.

The controversial opinions about the effectiveness of RON necessitated further investigations with larger patient populations. Opremcak et al. (2006a) evaluated the outcomes of RON in 117 patients with severe CRVO. They documented anatomic resolution in 95% of patients, and visual improvement of an average of 2.5 Snellen lines in 71% within 3 months postoperatively. Based on these favourable outcomes, they suggested RON might be a technically feasible and safe procedure that is more beneficial to patients with CRVO than the natural course of the disease. In a subsequent study carried out in the same year, Opremcak et al. (2006b) reported the results of RON combined with intraocular triamcinolone injections (RON/IOK) in 63 patients with CRVO and severe loss of vision. They observed anatomic resolution in 93% of patients and a visual gain of an average of 3 Snellen lines in 68%. These results were comparable with the outcomes of their previous series of 117 patients, who had undergone RON alone; however, RON/IOK was associated with a higher risk for IOP rise, which occurred in 25% of patients.

Improvements in VA after RON have been confirmed by several other reports, although none as encouraging as those of Opremcak et al. (2006a, 2006b). Weizer et al. (2003) performed RON in five eyes (four with CRVO, one with hemiretinal vein occlusion) and reported that VA improved in 80% of eyes postoperatively, but only 40% achieved VA of 20/80. Garcia-Arumi et al. (2003) prospectively evaluated the outcomes of RON in 14 patients with CRVO, and reported that 57.1% of eyes gained $\geq$ 1 line of vision after RON. Hasselbach et al. (2007) retrospectively analysed data for 107 patients with CRVO who underwent RON in the five ophthalmologic centres that collaborated in the German RON Study Group. Visual improvement of $\geq$ 2 lines was detected in 48.5% of all patients within 1 year postoperatively. However, only the non-ischaemic eyes achieved a statistically significant increase in VA compared with baseline values. Binder et al. (2007) evaluated the effectiveness of RON in 14 eyes with CRVO with VA $<$ 0.1 Snellen line. They reported visual improvement of $\geq$ 1 Snellen line in 43% of eyes, and a reduction in macular thickness as documented by optical coherence tomography (OCT) in 93%.

Martinez-Jardon et al. (2005) performed RON in 10 patients with ischaemic CRVO and found that, although resolution of macular oedema was documented by OCT in all eyes following RON, VA did not improve. These authors thus proposed that eyes with ischaemic CRVO would not benefit from RON. Similarly, in a study by Patelli et al. (2004), including five eyes with CRVO, resolution of macular oedema occurred in all eyes after RON, but was not accompanied by an improvement in VA.

Radial optic neurotomy has been reported to induce the development of retinochoroidal shunt vessels in 46.7–83.3% of patients (Azad & Verma 2003; Friedman 2003; Williamson et al. 2003; Nomoto et al. 2004; Spaide et al. 2004; Garcia-Arumi et al. 2007; Hasselbach et al. 2007). Hasselbach et al. (2007) defined those vessels as epipapillary or juxtapapillary vessels that are hyperfluorescent during the venous phase of FA and without leakage in late FA phases, suggesting that they were shunt or collateral vessels. They detected shunt vessels in 54.1% of 107 treated eyes after 3 months' follow-up and 70.4% after 6 months. They observed that patients

with shunt vessels at the neurotomy site showed a significantly better visual outcome, with a mean gain of 6 lines, in comparison with patients without these vessels, who achieved a mean gain of only 2 lines (Hasselbach et al. 2007). Garcia-Arumi et al. (2007) reported the incidence of retinochoroidal anastomoses after RON as 55% in both old and young age groups, including a total of 43 consecutive eyes with CRVO. Zambarakji et al. (2005) reported retinochoroidal shunt vessels in 60% of 10 patients after performing pars plana vitrectomy (PPV) and RON. Although OCT revealed a reduction in foveal thickness and macular volume following RON, they observed no visual benefit in eyes with shunt vessels compared with those without shunt vessels.

Nomoto et al. (2004) evaluated the effects of RON on retinal circulation by performing indocyanine green (ICG) videoangiography and computer-assisted image analysis in 15 eyes with CRVO. They showed that retinal circulation time decreased in all eyes after the development of chorioretinal anastomosis. These findings suggest that postoperative development of retinochoroidal shunt vessels seems to be the major factor influencing postoperative VA. These vessels contribute to visual improvement by draining retinal circulation to the choroid and accelerating the resolution of retinal oedema after RON. They may also decrease the risk of anterior segment neovascularization associated with CRVO (Nomoto et al. 2004; Spaide et al. 2004; Hasselbach et al. 2007). Furino et al. (2005) evaluated the synergetic effects of RON, PPV, ILM peeling and IVTA injection in eight patients with CRVO with best corrected VA < 20/200. At the end of the median follow-up of 5 months, mean VA improved to 20/200 in 87.5% of eyes, and anatomic resolution of intraretinal haemorrhages and vein congestion occurred in all eyes. Fluorescein angiographic evaluation revealed that perfused cases were observed to remain perfused, whereas indeterminate cases changed to perfused after RON. However, opposing those outcomes showing increased retinal perfusion after RON, Horio & Horiguchi (2006) detected a reduction in retinal blood flow following RON in a series of seven eyes with CRVO. This reduction occurred despite the presence of retinochoroidal shunt vessels, suggesting that chorioretinal anastomoses did not lead to an improvement in retinal blood flow. The authors suggested the development of severe gliosis and oedema at the neurotomy site or intravascular thrombus formation as possible reasons for the reduction.

In brief, RON was generally hypothesized to be effective as a result of the following pathophysiological mechanisms:

(1) relaxing the confined scleral outlet and increasing the retinal perfusion;
(2) inducing the formation of chorioretinal shunt vessels, thus draining retinal circulation to the choroid and accelerating the resolution of retinal oedema, and
(3) the additive positive effects of vitrectomy and/or removal of the ILM (Opremcak et al. 2001, 2006a, 2006b; Azad & Verma 2003; Friedman 2003; Garcia-Arumi et al. 2003; Williamson et al. 2003; Nomoto et al. 2004; Spaide et al. 2004; Furino et al. 2005; Martinez-Jardon et al. 2005; Hasselbach et al. 2007).

Radial optic neurotomy has been reported to cause various visual field defects. Hasselbach et al. (2007) detected visual field defects in 83.8% of 107 cases. These defects included unclassified scotomas in 42.6%, unspecific overall reduction of sensibility in 16.2%, and temporal and, especially, wedge-shaped visual field defects with possible correlation to the neurotomy site in 25% of cases. In order to prevent the loss of a functional visual field, they suggested performing the incision at the inferior sector of the optic disc, which would affect the less important superior quadrants of the visual field. However, the absence of preoperative standardized evaluations in Hasselbach et al. (2007) made it unclear whether the visual field defects were associated with RON or with CRVO itself. In their retrospective analysis of eight patients with CRVO or hemi-CRVO, Tsujikawa et al. (2006) detected temporal wedge-shaped visual field defects in 88% of patients. Although the temporal field defects were expected to cause visual disability, those defects secondary to RON were well tolerated by their patients. Williamson et al. (2003) reported segmental visual field loss in one of four patients following RON, suggesting damage to the ONH. By contrast with those investigations showing visual field defects, Opremcak et al. (2006a, 2006b) reported no visual field defects associated with RON in their series of 117 patients.

Although RON has been proposed as safe by most authors, the possibility of serious complications should not be overlooked. The procedure is performed in close proximity to the very delicate and critical structures of the ONH, and therefore carries a potential risk of laceration of the CRA or CRV, optic nerve fibre damage with visual field loss, globe perforation, retinal detachment, choroidal neovascularization at the neurotomy site and anterior segment neovascularization (Opremcak et al. 2001; Weizer et al. 2003; Martinez-Jardon et al. 2005).

Careful patient selection may provide better results after RON. Patients with pronounced peripapillary swelling at baseline and with an onset of CRVO of < 90 days were reported to be more likely to benefit from RON (Hasselbach et al. 2007). As a result, the benefits of RON appear to be controversial and its efficacy remains to be proven in prospective randomized clinical studies.

Chorioretinal venous anastomosis

Chorioretinal venous anastomosis, in which a shunt is performed between a retinal vein and the choroids, aims to bypass the occluded vein by an alternative route, improve retinal outflow and relieve the venous obstruction (Parodi et al. 2003; Sharma & D'Amico 2004). It can be induced by laser or by surgery. Laser-induced chorioretinal venous anastomosis was initially described by McAllister & Constable (1995) as a treatment modality for non-ischaemic CRVO. The treatment involved producing an intense focal laser burn of the retina at the edge of a chosen segment of vein by using a 50-μm spot size, 0.1-second duration and a power level of 1–4 W. McAllister et al. (1998) reported successful anastomosis formation in eight of 24 eyes (33%) with variable degrees of recovery of visual function. However, this treatment was frequently

associated with serious complications, including posterior vitreous detachment, choroidal or vitreous haemorrhages, preretinal fibrosis, choroidal neovascularization, segmental retinal ischaemia and retinal detachment (McAllister & Constable 1995; McAllister et al. 1998; Opremcak et al. 2001; Koizumi et al. 2002; Sharma & D'Amico 2004). High complication rates and low success rates limited the utility of laser-induced chorioretinal venous anastomosis.

Surgically induced chorioretinal venous anastomosis has been described by several authors. Fekrat & de Juan (1999) performed venipuncture to induce venous shunt in a case of ischaemic CRVO. In the same year, Peyman et al. (1999) described a new surgical technique to create chorioretinal venous anastomosis and achieved visual improvement in three of five patients (60%) with ischaemic CRVO. Their technique aimed to create a chorioretinal shunt by performing standard vitrectomy and Mersilene suture insertion beneath the retina, adjacent to the major retinal veins. Quiroz-Mercado et al. (2001) subsequently performed a modified surgical technique in two eyes with ischaemic CRVO. After vitrectomy and posterior hyaloid detachment, chorioretinal venous anastomosis was created with erbium:YAG laser. The authors reported that this technique successfully improved VA without any complications. Mirshahi et al. (2005) reported clinically successful shunt development in 90% and visual improvement in 80% of 10 patients. Their technique consisted of PPV with slit-like incisions through Bruch's membrane, adjacent to the partially cut major retinal veins in each quadrant. Mersilene sutures were inserted in the incised sites to induce chorioretinal venous shunt. However, Mirshahi et al. (2005) also experienced complications with this procedure in 30% of patients, including retinal detachment, vitreous haemorrhage and cataract. Koizumi et al. (2002) achieved successful chorioretinal venous anastomosis in 71% of seven consecutive patients with CRVO by cutting off the affected retinal vein by means of vitrectomy and making a small incision at both sides of the vein interruption through the full thickness of the retina, retinal pigment epithelium and Bruch's membrane. They proposed that complete interruption of the vein allowed the vein to connect to another venous route more easily, and vitrectomy reduced the incidence of neovascularization after chorioretinal venous anastomosis.

Although performing a surgically induced chorioretinal venous anastomosis does not lead to reperfusion of the areas with capillary non-perfusion, it is thought to reduce the ischaemia of parafoveal and perifoveal areas, leading to VA improvement resulting from the improved venous outflow and reduced macular oedema. It also reduces the risk of the development of neovascularization as a result of the vitrectomy performed (Peyman et al. 1999).

Vitrectomy with or without internal limiting membrane peeling

Different therapeutic options are available for the management of macular oedema, including observation for spontaneous resolution, systemic or local administration of drugs, and laser therapy. However, it often takes several months for macular oedema to resolve with these treatment modalities. As persistent macular oedema may lead to irreversible visual loss as a result of apoptosis of the photoreceptors, rapid resolution of macular oedema is mandatory for the preservation of VA (Liang et al. 2007). Pars plana vitrectomy with ILM peeling has been suggested as beneficial for the rapid resolution of retinal damage and macular oedema in patients with CRVO (Mandelcorn & Nrusimhadevara 2004; Furino et al. 2005; Liang et al. 2007). Although the exact mechanism by which ILM peeling reduces macular oedema is unclear, a number of possible mechanisms have been proposed, including the suggestion that ILM acts as a scaffold for proliferating astrocytes and its removal reduces vitreomacular traction and inhibits epiretinal membrane formation (Liang et al. 2007). As the Müller cell footplates make up the outer part of the ILM, their removal via ILM peeling is thought to induce gliotic response, which helps to release the extracellular fluid into the vitreous cavity by contracting the retinal layers and decreasing extracellular spaces (Furino et al. 2005). Furthermore, deroofing of the inner retina by ILM peeling may decompress the oedematous retina and facilitate the release of extracellular fluid and blood into the vitreous, which may help to restore normal retinal thickness, reduce opacities within the retina and interfere with light transmission to photoreceptors (Mandelcorn & Nrusimhadevara 2004). The effectiveness of ILM peeling may also reflect enhanced effects of IVTA injection and PPV (Mandelcorn & Nrusimhadevara 2004).

Mandelcorn & Nrusimhadevara (2004) performed PPV with ICG-assisted ILM peeling in 14 cases of macular oedema caused by CRVO or BRVO. Decreased retinal thickness and increased VA were observed in 78.6% of cases after the operation, which represented a better outcome than that described in the natural history data outlined by the Central Vein Occlusion Study Group (1997). Liang et al. (2007) also reported comparable outcomes after PPV, ILM peeling and scatter laser photocoagulation in 11 patients with macular oedema secondary to CRVO and BRVO. They observed visual improvement of ≥ 2 lines in 72.7% of cases, which was associated with a rapid reduction in macular thickness within 1 week postoperatively. As previously mentioned, Furino et al. (2005) and Binder et al. (2007) also reported favourable results after RON, PPV and ILM peeling in patients with CRVO. They attributed these successful outcomes not only to the effect of RON, but also to the synergetic effects of vitrectomy and ILM peeling.

Comparatively successful results have also been reported in vitrectomy without ILM peeling. Vitrectomy itself can provide resolution of macular oedema by removing VEGF and other cytokines within the vitreous cavity (Funatsu et al. 2003a, 2003b). It also enhances oxygen transport to the hypoxic retina and halts neovascularization induced by hypoxia in the posterior pole, although anterior neovascularization might still develop as a result of the low oxygenation of the peripheral retina (Stefansson et al. 1990).

Tachi et al. (1999) showed statistically significant visual improvement after vitrectomy in cases of CRVO (14 eyes) and BRVO (27 eyes). Similarly, Saika et al. (2001) reported a statistically significant improvement in VA

in 19 consecutive patients after vitrectomy with gas/air tamponade for macular oedema caused by BRVO.

In opposition to reports in favour of vitrectomy, several other authors do not confirm its benefits in eyes with CRVO (Radetzky et al. 2004; Hvarfner & Larsson 2006). Hvarfner & Larsson (2006) retrospectively evaluated the effectiveness of vitrectomy in eight eyes with non-ischaemic macular oedema secondary to CRVO and hemi-retinal vein occlusion. They reported that vitrectomy showed an initial positive effect for the resolution of macular oedema, but no beneficial effect in the longterm. Similarly, Radetzky et al. (2004) retrospectively analysed 23 patients who underwent PPV and ILM peeling for macular oedema secondary to CRVO, and reported an initial positive response to vitrectomy, but a less beneficial effect in the longterm. Radetzky et al. (2004) therefore proposed that vitrectomy and ILM peeling might be beneficial in the reduction of intraretinal oedema, but failed to identify the underlying the pathophysiological mechanisms such as growth factor expression or altered fluid dynamics.

Direct injection of tissue plasminogen activator via retinal vein cannulation

In previous years, systemic or intravitreal administrations of t-PA to recanalize the obstructed vein have been investigated. The systemic administration of thrombolytic agents to treat CRVO showed beneficial effects on retinal blood flow in some cases, but was associated with the risk of massive vitreous haemorrhage and serious systemic complications, including patient mortality (Elman 1996; Lahey et al. 1999; Weiss & Bynoe 2001). Intravitreal injection of t-PA also did not have a beneficial effect on the course of CRVO and resulted in worsened vision in some cases (Lahey et al. 1999; Sharma & D'Amico 2004). These unsuccessful results with systemic and intravitreal injections promoted investigations for different routes of t-PA administration. Weiss & Bynoe (2001) described a novel surgical procedure which allowed direct administration of t-PA into the affected retinal vein. Their surgical technique included PPV with posterior hyaloid removal, followed by cannulation of a peripapillary retinal vein branch and injection of a bolus of 200 μg/ml t-PA towards the ONH. They suggested that this technique provided several advantages over other methods of t-PA delivery:

(1) t-PA was delivered to precisely where it was required to cause rapid lysis of the thrombus;
(2) direct visualization of the drug reaching the site of thrombus was possible;
(3) administration of a very small dose could provide a sufficient concentration near the thrombus, and
(4) depending on its flow rate, the injection could cause a flushing effect, dislodge the thrombus and allow dilation of the CRV.

Weiss & Bynoe (2001) reported visual improvement in 54% of 28 eyes with CRVO with this technique. Similarly, Bynoe et al. (2005) obtained favourable results with this surgical technique in 25 patients with CRVO. They reported visual recovery of 3 lines in 72% and 8 lines in 36% of eyes. Recently, Feltgen et al. (2007) also treated 13 patients with ischaemic CRVO using retinal endovascular lysis, as described by Weiss & Bynoe (2001). However, by contrast with previous studies, they reported a disappointing visual outcome and high complication rates with this surgical technique.

Direct injection of t-PA via retinal vein cannulation is a feasible technique; however, it can lead to serious ocular complications, including vitreous haemorrhage, retinal tear formation, retinal detachment, neovascular glaucoma, endophthalmitis and phthisis bulbi. Although the complication rate was considered reasonable by Bynoe et al. (2005), it was found to be unacceptably high by Feltgen et al. (2007).

Conclusions

None of the treatment procedures have been found to effectively prevent visual loss or retrieve lost vision after CRVO. Treatments that target the complications of venous occlusion, such as grid laser photocoagulation for macular oedema and prophylactic panretinal laser photocoagulation for non-perfused CRVO, were shown to be ineffective in improving vision. Attempts to bypass the venous obstruction by using laser chorioretinal venous anastomosis have been performed with limited success and significant complications. Close observation, which is suggested by the Central Vein Occlusion Study Group (1993, 1997) as well as by most of the authors dealing with CRVO, is still the main point in treatment. However, vein occlusion with macular oedema has a significant impact on quality of life, and most patients are willing to undergo potentially invasive treatment to resolve it (Chang et al. 2007).

In conclusion, surgical treatment options for CRVO seem to be promising, although it remains unclear whether or not the outcomes of these surgeries are superior to those of the natural history of the disease. Most studies that have evaluated the effectiveness of these surgeries have consisted of interventional case series without control groups, and their outcomes are compared with those of the (Central Vein Occlusion Study Group (1993, 1997). However, the CRVO study only included cases with $\geq$ 3 months duration, whereas the investigational case series included many cases with shorter duration of CRVO (Weizer et al. 2003; Patelli et al. 2004; Martinez-Jardon 2005). All differences in follow-up times, initial treatment times, ischaemic/non-ischaemic status of cases and the various durations of CRVO prevent accurate comparisons between the outcomes of interventional case series and the studies performed by the Central Vein Occlusion Study Group (1993, 1997). As previous review articles have stressed, surgical treatment options for CRVO are at present experimental and well designed prospective trials supporting these surgeries are still lacking (Shahid et al. 2006; Mohamed et al. 2007). Hence multicentre, randomized, controlled trials evaluating each of these surgical options are mandatory if we are to establish standard guidelines for the treatment of CRVO.

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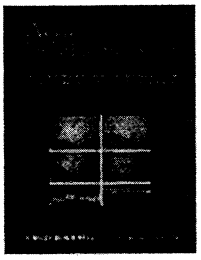

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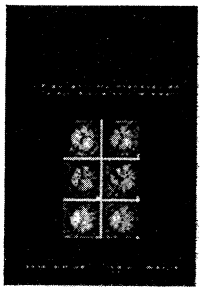

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⇒ **Surgical treatment of central retinal vein occlusion**
Nilufer Berker and Cosar Batman

Berker & Batman, in Ankara, review several approaches to the surgical treatment of central retinal vein occlusion.

Visual fields in children with attention-deficit / hyperactivity disorder before and after treatment with stimulants
Lene Martin, Eva Aring, Magnus Landgren, Ann Hellström and Marita Andersson Grönlund

Children with attention-deficit/hyperactivity disorder (ADHD) showed better visual acuity (VA) and visual fields (VF) results with than without psychostimulant medication.

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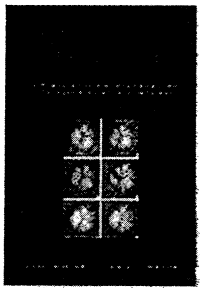

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