

Combined retinal vascular occlusion: Demography, clinical features, visual outcome, systemic co-morbidities, and literature review

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Purpose: To document the clinical features, systemic association, and treatment outcome of patients with a combined retinal vein and artery occlusion (CRVAO) and review of literature. **Methods:** A retrospective chart review of patients diagnosed with CRVAO at a tertiary eye care center. Patient's demographic details and associated ocular and systemic factors were recorded. Treatment included laser photocoagulation, anti-vascular endothelial growth factor (VEGF) intravitreal injection or transscleral cyclophotocoagulation (TSCPC), alone or in combination. At last, follow-up treatment response was measured in visual acuity status, regression of neovascularization, and control of intraocular pressure (IOP). All cases reported in the current decade were analyzed and compared with this study. **Results:** Seventeen eyes with CRVAO accounted for 0.3% of total vascular occlusion (total 5151 patients were seen in this period). The mean age was 48.12 ± 17.5 years (range: 12-87 years) and there were 9 females. Nine eyes had CRVO + CRAO; 6 eyes had BRVO + BRAO, and one patient each had CRVO + BRAO and CRAO + BRVO. Fluorescein angiography (FA) showed delayed 'arm to retina' time (>20 seconds) in all 10 eyes and delayed arteriovenous transit time in 9 out of 10 eyes. Optical coherence tomography (OCT) showed hyporeflective inner retinal layers (16 eyes) and neurosensory detachment (7 eyes). The most common systemic associations were hypertension and dyslipidemia ($n = 7$ people; 41.18%) each. Four patients (23.5%) had a plaque in carotid arteries with normal 2D echocardiography. Ten (59%) eyes were treated with intravitreal bevacizumab + laser; four (23.5%) eyes were treated with laser only, and three (17.6%) eyes were treated with laser + anti-VEGF + TSCPC. At last follow up, vision improved in 9 (52.9%) eyes; stable in 3 (17.7%) eyes, and reduced to perception of light in 5 (29.4%) eyes. **Conclusion:** Combined CRVAO is a rare emergency leading to acute vision loss. Early diagnosis and treatment for ocular complications and systemic evaluation for cardiovascular risk factors are needed.

Key words: Cardiovascular factors, combined retinal artery and vein occlusion, intravitreal bevacizumab, laser photocoagulation

Combined retinal vascular occlusions involving the vein and the artery is a rare event. Traditionally, the retinal vein occlusions are classified into branch retinal vein occlusion (BRVO), macular vein occlusion, central retinal vein occlusion (CRVO), and hemi central retinal vein occlusion (HCRVO); the retinal artery occlusions are classified into central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and cilioretinal artery occlusion (CLRAO). The combined vein and artery occlusion could be any permutation and combination such as CRVO + CRAO, CRVO + BRAO, BRVO + CRAO, and BRVO + BRAO.^[1-3] Majority of patients suffer from CRVO + CRAO, and occasionally with CLRAO or BRAO.^[4,5] The less common reported entity is BRVO + BRAO.^[6] A variety of pathological mechanisms are described for these combined occlusions. A sudden increase in intraluminal retinal capillary bed pressure secondary to CRVO could lead to CLRAO.^[7] Similarly reduction in perfusion pressure of the cilioretinal and retinal arteries, in turn, leads to decreased retinal circulation and subsequent venous stasis and

thrombosis. Many systemic co-morbidities associated with retinal vein occlusions—atherosclerosis, hypertension, hyperlipidemia, diabetes, and hyperhomocysteinemia in people aged above 50 years^[8] and thrombophilic disorders, hyperviscosity blood disorders, systemic vasculitis, and autoimmune diseases in people aged less than 40 years^[9]—could damage the adjacent artery to cause combined vascular occlusion. The commonly reported systemic associations are diabetes, hypertension, and dyslipidemia.^[10,11]

In general, the prognosis of patients with combined vascular occlusion is poor. Majority of the eyes develop severe complications, such as rubeosis iridis and neovascular glaucoma.^[12,13] Therefore, early diagnosis and intervention are needed.^[6] Considering the rare nature of the disease and very

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few anecdotal case reports,^[1-4] and short case series^[6] published in the literature, the current understanding of this disease is very limited. This article describes the clinical profile, imaging features, associated systemic co-morbidities, complications and visual outcomes in patients of the combined retinal vein and artery occlusion (CRVAO). This article has also compiled the reports of combined vascular occlusion in this decade and compared it with the present series.

Methods

In a retrospective chart review of all patients diagnosed with combined retinal vein and retinal artery occlusion between January 2016 and December 2018 at a tertiary eye care institute were included. We used electronic medical records to get ICD coding for both retinal artery (H 34.1) as well as retinal vein occlusion (H 34.2 and H 34.8) to identify our study population. The diagnosis was made by clinical examination and specific retinal investigations. Inclusion criteria included patients who were diagnosed to have acute and recent onset of combined vascular occlusion. We excluded cases who presented with sequential or late-onset of combined vascular occlusion. Patients with ocular ischemic syndrome, diabetic retinopathy, hypertensive retinopathy, and other co-existing ocular disorders were also excluded from the study. Informed consent was obtained from all patients and the study was approved by the institutional ethics committee. The study adhered to the tenets of the Declaration of Helsinki of medical research involving human subjects.

Demographic details like age at presentation, sex, eye involved, and types of occlusion were recorded. The patients were categorized into two age groups: group 1 below 40 years and group 2 above 40 years. A thorough review of the patient's medical chart was made at baseline and at every follow-up visit. It included presenting and best-corrected visual acuity, anterior segment examination including the presence of iris neovascularization (NVI), measurement of intraocular pressure (IOP) by Goldmann applanation tonometer, gonioscopy, and a dilated fundus examination. Special ophthalmic examinations included fluorescein angiography (FA) and optical coherence tomography (OCT). FA recorded the arm-to-retina time (in seconds), the distribution of capillary nonperfusion (CNP) areas and presence of new vessels elsewhere (NVE) on the retina, new vessels on disc (NVD), new vessels on iris (NVI), and cystoid macular edema (CME). OCT documented the presence of hyporeflective nerve fiber layer; this confirms the occurrence of arterial occlusion even in the presence of significant retinal hemorrhages secondary to vein occlusion. The macular cube OCT qualified and quantified macular edema, when present.

A detailed systemic examination by an internist documented systemic disease, if any. Pertinent personal history such as cigarette smoking was noted. Blood pressure was measured using a manual sphygmomanometer in a sitting position. Blood investigations included complete blood count, fasting and postprandial blood sugar, complete lipid profile, renal profile, coagulation profile, and serum homocysteine were performed in all patients as per the institution protocol for all vascular disease. Autoimmune disease workup was ordered in all people aged below 40 years. Systemic investigations also included carotid doppler ultrasonography, and 2 D

echocardiography. Patients with either carotid artery disease or abnormal echocardiography were referred to cardiologist for further evaluation. In subsequent follow-up visits search was made for NVE, NVD, NVI, and neovascular glaucoma (NVG). NVG was diagnosed by the presence of NVI and new vessels in angle (NVA) leading to secondary open or closed-angle associated with elevated IOP (>21 mm Hg) in the presence of posterior segment ischemia.

Eyes that had either cystoid macular edema or ocular neovascularization in form of NVI, NVA, or NVE at the time of presentation were appropriately treated with laser photocoagulation (PHC) and/or intravitreal anti-vascular endothelial growth factor (VEGF) therapy where visual potential existed, and transscleral diode laser cyclophotocoagulation (TSCPC)/cyclocryotherapy when the visual potential did not exist.

All patients were followed up for a minimum duration of 3 months and essential outcome parameters were recorded, such as improvement (2 or more Snellen's line) or stabilization of vision, and IOP. All complications, either secondary to disease or treatment *per se*, were also recorded.

Literature review for all the CRVAO cases based on a PUBMED database search, using the terms combined retinal vascular occlusion, central retina artery and vein occlusion, and branch retinal artery and vein occlusion in the current decade (2009-2018) were reviewed and compared with our study.

Results

In the study period of 3 years, 5151 people were treated in the institute for retinal vascular occlusion. This included 4377 (85%) people with vein occlusion and 774 (15%) people with artery occlusion. In the study period, 17 patients (17 eyes) were diagnosed to have combined retinal artery and vein occlusion; this study included these consecutive patients. This was 0.3% of all retinal vascular occlusion in this period and consisted of CRVO + CRAO in 9 patients [Fig. 1- Case 2], BRVO + BRAO in 6 patients [Fig. 2- Case 6], CRVO + BRAO in one patient and BRVO + CRAO in one patient. Cilioretinal artery occlusion was not seen in any patients (confirmed on FA). The mean age of the patients was 48.12 ± 17.5 years (Interquartile range: 35.5-56.2 years, range: 12-87 years), there were 9 females, and the left eye was affected in 12 (70.6%) patients. Twelve patients were aged above 40 years and 5 people were under 40 years. At presentation, IOP was greater than 21 mm Hg in 2 (11.7%) eyes. The super temporal quadrant vessels, both vein and artery, were involved in 5 of 6 eyes in combined BRVO and BRAO occlusions. Three eyes had cystoid macular edema (2 eyes with BRVO + BRAO and one eye with CRVO + CRAO). In all patients, the other eye was normal with mild hypertensive changes. The presenting best-corrected visual acuity was $\leq 20/200$ in 13 patients. In 3 months follow up, 10 eyes developed ocular neovascularization as follows: NVI in 6 eyes and NVD + NVE in 4 eyes. Thirteen eyes received intravitreal bevacizumab injection, 10 eyes with ocular neovascularization, and 3 eyes with cystoid macular edema. Finally, 7 eyes developed NVG and 2 eyes developed vitreous hemorrhage. The mean duration of follow-up was 11 months (range 3-24 months). The complete demographic and clinical details are shown in Table 1.

On FA (10 eyes), there was delayed arm to retina time (>20 seconds) in all 10 eyes, delayed arteriovenous (AV) transit time in 9 eyes, and presence of 2 or more quadrant CNP areas in 10 eyes. OCT showed hype reflective inner retinal layers in 16 eyes, neurosensory detachment in 7 eyes, macular edema in 3 eyes, and inner retinal layer atrophy in one eye.

On systemic evaluation, 7 (41.8%) people each had hypertension and dyslipidemia, 4 (23.5%) people each

had diabetes mellitus and hyperhomocysteinemia, and 1 person (case no-11, age 12 years) had autoimmune disease (lupus coagulopathy) associated with thrombosis. In patients less than 40 years of age ($n = 5$; CRVO + CRAO), there was anemia with leucopenia ($n = 2$), anemia with thrombocytopenia ($n = 1$), antiphospholipid antibody syndrome ($n = 1$), and dyslipidemia ($n = 1$). On carotid doppler ultrasonography, 4 people showed plaque formation on the same side of occlusion (2 fibro-fatty plaque and 2 calcific plaque in carotid artery) with stenosis in internal carotid or common carotid artery ranging from (22% to 51%); 2 D echocardiography didn't show vegetation or embolic material on any of heart valves. In 3 patients ocular or systemic risk factors could not be identified despite complete blood investigations and multimodal imaging. Two of the 3 eyes had NVD and NVE and in both of them, vision did not improve after treatment.

The treatment in the current cohort consisted of combination of intravitreal anti VEGF (bevacizumab 1.25 mg in 0.05 ml) with pan retinal photocoagulation (PRP) in 7 (41%) eyes for regression of NVD/NVE; anti VEGF with sectoral laser PHC in 3 eyes (17%) for associated macular edema; sectoral laser PHC alone in 4 (24%) eyes, and combination of laser, anti-VEGF and TSCPC in 3 (17%) eyes. Three eyes that had gross CNP areas, but no NVE or macular edema, were still treated with retinal laser to prevent development of retinal new vessels as suggested in one earlier report from India.^[6] At the last follow up, the best corrected visual acuity showed improvement of 2 or more Snellen's line in 9 (52.9%) patients; remained stable in 3 (17.7%) patients, and reduced to perception of light in 5 (29.4%) patients [Table 1].

In this decade, 2009-2018 a total of 41 cases are reported; this consists of 3 case series (24 cases)^[6,10,11] and 17 case reports^[14-28] of CRAO published in English language (PubMed search). In the isolated case reports of 17 patients, the mean patient age was

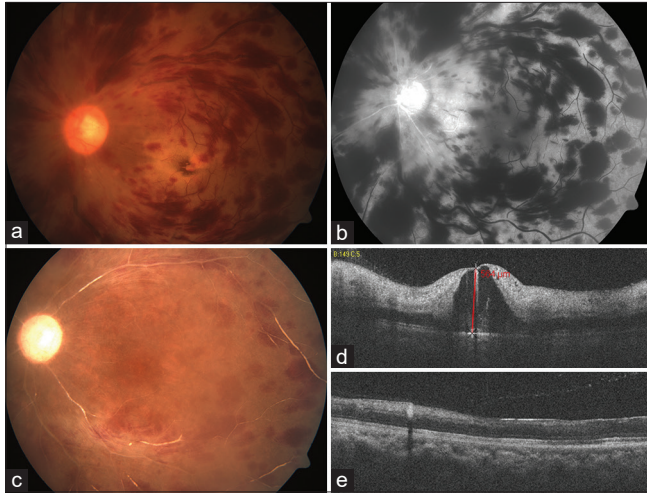


Figure 1: Case 2. (a) Left eye with combined central retinal vein and artery occlusion with a cherry red spot at the macula. (b) FA in late phase showed hypofluorescence areas with no evidence of dye in retinal vessels except small perfused area supplied by the cilioretinal artery. (c) Fundus at the last follow-up showed optic atrophy with sclerosed retinal vessels with gross macular ischemia. (d) OCT at presentation showed hyperreflective inner retinal layers with neurosensory detachment. (e) OCT at the last follow-up showed complete atrophy of inner retinal layers with thin epiretinal membrane

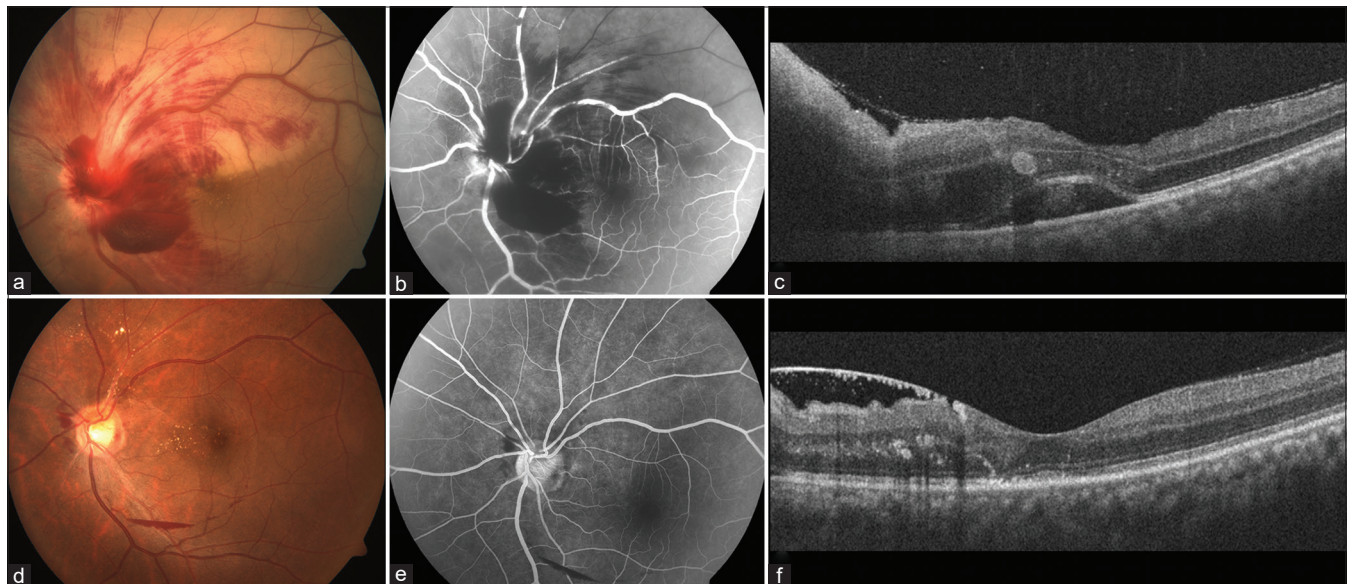


Figure 2: Case 6. (a) Left eye with superotemporal quadrant combined branch retinal artery and vein occlusion. (b) FA in the late phase showed blocked fluorescence with blockage of dye in peripheral retinal arteries. (c) OCT showed hyperreflective inner retinal layers with neurosensory detachment involving the fovea. (d) Fundus at last follow-up showed resolution of hemorrhage with complete perfusion of retinal vessels. (e) FA in the late phase showed reperfusion of dye in all retinal vessels with few areas of stippled isofluorescence. (f) OCT at last follow-up showed normal foveal contour with the resolution of edema

Table 1: Clinical profile, systemic associations, treatment and outcomes of the patients of CRVAO

#	Age/ Sex	Eye	Syst Dis	Carotid Doppler	Occlusion type	Eye at presentation			Treatment			FU Follow up (months)	Fellow Eye					
						BCVA	IOP	Neovascularisation	FA (Arm- retina time)	OCT (NFL edema)	Macula			VH	Anti VEGF	Other	IOP	BCVA
1	52/M	LE	HTN	Left side atheromatous thickening with calcific plaque	CRVO + BRAO	CFIM	19	YES, NVI	25 sec	YES	-	NO	YES	TSCPC PRP	60	HM	9	N
2	34/F	LE	C	NORMAL	CRVO + CRAO WITH CILIORETINAL SPARING	HM	12	YES, NVE	21 sec	YES, NSD	-	YES	YES	PRP	14	CFCF	8	N
3	31/F	LE	C	NORMAL	CRVO + CRAO	PL PR Acc	13	YES, NVI, NVD	--	YES	-	NO	YES	Sc LASER	22	HM	6	N
4	67/M	LE	DM	Minimal hyperplasia with fibrofatty plaque	CRVO + CRAO	CFIM	50	YES, NVI	32 sec	YES	-	NO	YES	Sc LASER	52	CFCF	3	N
5	54/M	LE	DM, HTN	NORMAL	STQ BRVO + BRAO	CF IM	14	YES, NVE	20 sec	YES	-	YES	YES	Sc LASER	16	20/50	5	N
6	46/M	LE	HTN	NORMAL	STQ BRVO + BRAO	20/40	10	NO	21 sec	YES, NSD, CME	-	NO	YES	Sc LASER	15	20/20	5	N
7	52/F	LE	-	NORMAL	ITQ BRVO + BRAO	20/400	16	NO	20 sec	YES, NSD, CME	-	NO	YES	Sc LASER	16	20/50	15	N
8	87/F	RE	-	NORMAL	ITQ BRVO + CRAO + GLAUCOMA	20/80	11	NO	--	YES, NSD	-	NO	--	Sc LASER	36	PL PR Inacc	19	N
9	45/F	RE	D	NORMAL	CRAO + CRVO	CFIM	14	NO	--	YES, CME	CME	NO	YES	Sc LASER	17	20/100	21	N
10	28/F	LE	C	NORMAL	CRAO + CRVO	HM	11	YES, NVI	22 sec	YES, NSD	-	NO	YES	TSCPC PRP	41	PL PR Inacc	7	N
11	12/M	LE	Lupus coagulopathy	NORMAL	CRAO + CRVO	CFCF	17	YES, NVI	--	YES, NSD	-	NO	YES	PRP	1	HM	24	N
12	47/M	RE	HTN, D, HH	NORMAL	STQ BRVO + BRAO	20/30	14	NO	20 sec	YES, NSD	-	NO	--	Sc LASER	13	20/20	10	NAAION
13	36/M	LE	D, HH	NORMAL	CRAO + CRVO	20/200	16	NO	--	YES	Cherry red spot	NO	--	Sc LASER	19	20/20	3	N
14	67/F	RE	DM, HTN, D	Intraluminal eccentric fibrofatty plaque in RT proximal common carotid	CRAO + CRVO	PL PR Inacc	42	YES, NVG	20 sec	YES	-	NO	YES	PRP + TSCPC + ARC	23	PL PR Inacc	11	Glaucomatous cupping
15	63/F	LE	DM, HTN, D	CALCIFIC PLAQUES	CRAO + CRVO	PL PR Inacc	30	YES, NVI	--	YES	-	NO	YES	PRP	21	NPL	19	N
16	52/F	LE	D, HH	NORMAL	STQ BRVO + BRAO	20/320	13	YES, NVD	--	YES, NSD	-	NO	YES	PRP	10	20/50	3	N
17	45/M	RE	HTN, D, HH	NORMAL	STQ BRVO + BRAO	20/25	10	NO	18 sec	NO,	ATROPHY	NO	--	Sc LASER	12	20/25	3	N

ARC: Anterior Retinal Cryotherapy, Acc: Accurate, BCVA: Best corrected visual acuity, C: Coagulation disorder, CFIM: Counting fingers at 1 metre, CFCF: Counting fingers close to face, CME: Cystoid macular edema, DM: Diabetes mellitus, D: Dyslipidaemia, F: Female, HH: Hyperhomocysteinemia, HM: Hand movement, ITQ: Inferotemporal quadrant, Inacc: Inaccurate, LE: Left eye, M: Male, NVI: Neovascularisation of the iris, NVD: Neovascularisation of the disc, NVE: Neovascularisation elsewhere, NVG: Neovascularisation glaucoma, NPL: Non-perception of light, N: Normal, NAAION: NonArteritic Anterior Ischemic Optic Neuropathy, NFL: Nerve fibre layer, PL PR: Perception of light and rays, PRP: Pan retinal photocoagulation, STQ: Supero-temporal quadrant, Sc LASER: Sectoral LASER, TSCPC: Transscleral cyclo diode photocoagulation, VEGF: Vasular endothelial growth factor

Table 2: Summary of published CRVAO reports from 2009-2019

No eyes	Type (n)	Av age (range)	M/F	Systemic risk factors	Presenting VA (<20/400)	Treatment	Complications	Post Rx VA
Case Reports^[14-28]								
17	BRVO + BRAO (n=3)	39.6 (27-54)	3:0	Toxoplasmosis, Peripapillary arterial loop, Hyperhomocysteinemia	02	Anti-toxo treatment and oral steroids	Retinal atrophy (1) NVG (1)	>20/200=02 Improvement
	CRVO + BRAO (n=2)	41 (16-66)	0:2	Hyperhomocysteinemia	01	Oral steroids + PRP (1)	NVG (1)	>20/200=0 worsened
	CRVO + CRAO (n=6)	43.6 (3-72)	1:5	Chronic renal failure, Factor V mutation, Nephrotic syndrome, Persistent hyaloid artery, Protein C deficiency, Systemic lupus erythematosus	06	Oral steroids (1) Anticoagulants (2)	NVG (1) Optic atrophy (1)	>20/200=02
	CLRAO + CRVO (n=6)	24.1 (9-45)	4:2	Sturge Weber Syndrome, Sleep apnea syndrome, HELLP syndrome, Hyperhomocysteinemia, Juvenile glaucoma, Post-partum	01	AGM (1) Trabeculectomy (1) PRP (1)	NA	>20/200=04 Improvement
Case Series^[6,10,11]								
24	BRVO + BRAO (n=6)	54 (39-60)	5:1	Dyslipidemia (5), Hypertension (4), Diabetes (4), Hyperhomocysteinemia (1)	04	Laser PRP (6), PRP + Avastin (3)	CME (2 eyes), Macular ischemia (2 eyes) NVD/NVE (2 eyes), TRD (1 eye)	>20/200=04 Improvement (4) Stable (2)
	CRVO + BRAO (n=3)	48.3 (33-64)	2:1	Hypertension (2), Chronic smoker (2), Coagulation disorder (1)	03	Anticoagulants (1) Antihypertensive (2)	NA	>20/200=01 Improvement (1) Stable (2)
	CRVO + CRAO (n=10)	62 (36-75)	6:4	Hypertension (6), Coagulation disorders (5), Dyslipidaemia (3), Hyperhomocysteinemia (2)	10	Anticoagulants, hemodilution Vitrectomy (1)	NA	>20/200=06 Improvement (6) Stable (3) Worsened (1)
	CLRAO + CRVO (n=5)	41.4 (3-82)	4:1	Hypertension (3), Smoking (3) Dyslipidaemia (2), Hyperhomocysteinemia (1)	03	Low molecular heparin and acetylsalicylic acid (5)	NA	>20/200=01 Not mention in 4 eyes
Present series								
17	BRVO + BRAO (n=6)	49.3 (45-54)	4:2	Hypertension (4), Dyslipidemia (3), Hyperhomocysteinemia (3)	03	Avastin+PRP (4) Sectoral laser (2)	CME (3) NVE (1) NVD (1) Foveal atrophy (1)	>20/200=06 Improvement (5) Stable (1)
	CRVO + BRAO (n=1)	52	1:0	Hypertension, Carotid: calcific plaques	HM+	PRP+TSCPC	NVE, NVG	PL+Worsened
	CRVO + CRAO (n=9)	42.5 (12-67)	3:6	Dyslipidemia (4), Hypertension (2), Diabetes (3), Coagulation disorders (3) Carotid: fibro fatty plaque (2) and calcific plaque (1)	08	PRP + Avastin (6) Sec laser (1) PRP + Avastin + TSCPC (2)	NVI (5) NVG (1) Vit hemorrhage (1)	>20/200=02 Improvement (2) Worsened (7)
	BRVO + CRAO (n=1)	87	0:1	Primary open angle glaucoma	20/80	Sectoral laser	NVG	PL+Worsened

35.7 years (range 3-72 years) and the most common occurrences were of CRVO + CRAO ($n = 6$) and CLRAO + CRVO ($n = 6$) with a variety of systemic disorders known to cause CRVAO [Table 2]. In the case series of 24 patients the average age was 54.3 years, and the leading systemic associations were hypertension ($n = 15$) and dyslipidaemia ($n = 10$). The presenting vision was poor (VA <20/400) in 30 of 41 (73%) patients. The management consisted of systemic and ocular treatment: systemic antihypertensive, anticoagulants and ocular- laser photocoagulation and/or intravitreal anti-VEGF injection. At the final follow up vision improved in only 50% cases ($n = 20$) and remained stable in other half of the patients [Table 2].

Discussion

In our series, the patients presented with 4 different types of CRVAOs: CRVO with CRAO, CRVO with BRAO, BRVO with BRAO and CRAO with BRVO. Most patients ($n = 12$; 70%) in this cohort were aged above 40 years.

Combined arterial and venous blockage is reported to occur in both young and old people and many of them with systemic comorbidities.^[6] The important systemic association reported with CRAO are advanced age, hypertension, hyperlipidemia, diabetes, and glaucoma in the older age group (>40 years),^[8] and inherited and acquired coagulation disorders and hyperviscosity syndrome-related factors in younger age group (<40 years).^[9] All these conditions generate one or other factors of Virchow's triad—hypercoagulability, damage to the vessel endothelium, and hemodynamic changes such as venous stasis or turbulence. These features ultimately contribute to venous thrombosis formation thereby causing arterial obstruction by back pressure leading to combined arterial and venous occlusion.^[7] In majority of cases in the elderly population, retinal vein occlusion is the primary pathology. Due to atherosclerotic changes in the arteries, the vein gets compressed usually at arteriovenous crossing leading to turbulent blood flow and dynamic obstruction or actual thrombus formation and mechanical blockage. The increased intravascular pressure may cause back pressure to the arterial circulation leading to artery occlusion.^[6]

In 4 of our elderly patients, the carotid doppler showed the presence of plaque and one of the other risk factors such as hypertension, diabetes, or dyslipidemia. All these 4 patients had NVI or NVE at follow-up visit and despite laser and/or anti-VEGF therapy all eyes had a poor vision (less than hand movements) on the last visit. This was in contrast to 7 other patients who also had systemic diseases (hypertension, diabetes or dyslipidaemia) but without the presence of plaque on carotid doppler; in these patients, vision either improved ($n = 6$) or remained stable ($n = 1$) following laser and/or anti-VEGF therapy. Thus, the combination of plaque on carotid and advanced age could be considered a bad prognostic indicator for visual acuity.

In the younger age group, coagulation disorders like anticardiolipin syndrome, von Willebrand syndrome, protein S deficiency, or Factor V mutation are known risk factors for combined occlusion.^[22,29] The postulated mechanism is that the hypercoagulable blood state predisposes to venous thrombosis and increased back pressure to the arterial circulation leads to artery occlusion. In our series 2 patients had hyperviscosity related disease, both in their 30s while one young child age 12 years (case no-11) was diagnosed

to have lupus coagulopathy with thrombosis. Both of them received anti-VEGF injection with sectoral laser PHC and at the last follow up the new vessels regressed, confirmed by fluorescein angiography. It appears that younger people with hyperviscosity related disease have a better visual prognosis than the older patients with arterial plaques.

One elderly patient had pre-existing advanced primary open-angle glaucoma. Despite laser treatment, the IOP remained uncontrolled and vision was poor at the last follow-up visit. The postulated mechanism is either the rise in the IOP above the mean blood pressure or the fall in blood pressure below the IOP leads to decrease retinal blood flow in the artery, and consequent occurrence of transient CRAO^[7] that typically lasts for several hours, mostly during sleep due to marked nocturnal arterial hypotension.

In 3 patients, ocular or systemic risk factors could not be identified despite complete blood investigations and multimodal imaging. The occurrence of CRVAO is also reported in otherwise healthy subjects^[30,31] although we suspect that some of these patients in the reported series may not have undergone complete diagnostic tests including transesophageal echocardiography, cerebral magnetic resonance imaging (MRI), and thrombophilia screening. Thus, it is important to consider uncommon (e.g., Flammer syndrome) or common but so far unrecognized (e.g., fluctuation of blood pressure) risk factors for CRVAO in such people.^[11]

Typically, eyes with CRVAO have a poor visual outcome and tend to develop complications like NVI and NVG^[2] and if untreated, could lead to complete blindness.^[10] The ongoing activity of neovascularization due to continuous hypoxia from occlusion and increasing VEGF levels in the vitreous cavity remains the cornerstone for the complications. In our study, 10 (58.8%) eyes had complications like vitreous hemorrhage (2 eyes), NVD (2 eyes), NVE (2 eyes), NVI (6 eyes), and NVG (7 eyes).

The current standards of care in CRVAO are anti-VEGF and laser photocoagulation, often in combination and occasionally TSCPC when other treatment fails to prevent NVG.^[32] Intravitreal anti-VEGF reduces the VEGF levels and laser PHC reduces retinal ischemia. In our cohort of people, vision either improved or remained stable in 2/3rd of eyes and vision deteriorated in 1/3rd of eyes. Therefore, treatment must be instituted as soon as the diagnosis is made.

The analysis of 41 published cases in this decade [Table 2] showed that the incidence of CRVAO is rarer than isolated retinal vascular occlusion, the occurrence is usually acute, there is significant vision loss at presentation, and the treatment benefit is maximized with early management including care for systemic commodities. The analysis further showed that the people with CRVAO were younger than isolated vein occlusion (average 45.6 years versus average 60 years)^[33] and the risk of NVG is higher than the isolated artery or vein occlusions (50% versus less than 20%).^[34,35]

Conclusion

To summarize, CRVAO is an ocular emergency presenting with painless sudden vision loss. Clinical examination supplemented with Fundus fluorescein angiography (FFA) and OCT help in confirming the diagnosis. A thorough

systemic evaluation is mandatory to look for atherosclerosis, hypertension, dyslipidemia, and diabetes in the elder people and coagulation and hyperviscosity syndrome in younger people. In majority of instances, ocular neovascularization occurs that must be treated with laser photocoagulation and intravitreal anti-VEGF injection alone or in combination, and occasionally TSCPC for control of glaucoma. Therefore, an early diagnosis, adequate treatment, and timely referral to internist/cardiologist to rule out high-risk factors could help salvage vision in many of these eyes.

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Conflicts of interest

There are no conflicts of interest.

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