

Predictive Factors for Visual Prognosis in Patients with Central Retinal Vein Occlusion at Thammasat Eye Hospital

Bottomalen Sorn¹, Krytha Tor¹, Remy Tor¹, Guechlaing Chea¹, Juraiporn Suntirumjairucksak², Navapol Kanchanaranya²

^{1, 2, 3, 4}Ophthalmology Department, Preah Ang Duong Hospital, Phnom Penh, Cambodia

⁵ Ophthalmology Department, Thammasat University Hospital, Pathum Thani, Thailand

Abstract: *This retrospective study evaluated factors predicting visual prognosis in 68 patients with central retinal vein occlusion treated at Thammasat Eye Hospital between January 2017 and December 2018. Patients were divided into younger than 50 years and 50 years or older. Clinical characteristics, systemic risk factors, treatment, and visual outcomes were analyzed. Most patients received intravitreal anti-VEGF therapy, while pan-retinal photocoagulation was performed when neovascularization developed. Significant visual improvement was observed during follow-up. Hypertension was the most common systemic risk factor. Better visual outcomes were associated with younger age, male sex, treatment initiated within 30 days of symptom onset, and non-ischemic CRVO. These findings may assist clinicians in predicting visual prognosis and optimizing patient management.*

Keywords: Central retinal vein occlusion; Visual prognosis; Anti-VEGF; Macular edema; Retinal ischemia; Risk factors.

1. Introduction

Retinal vein occlusion (RVO), having a prevalence rate of 0.1 - 0.2%, presents as one of the most common retinal vascular diseases in elders. There are many ophthalmic and systemic risk factors of RVO such as; cardiovascular disease and certain coagulopathies [1]. It is important to distinguish ischemic from non-ischemic central retinal vein occlusion because it helps to predict the risk of ocular neovascularization, to identify the prognosis, to determine the spontaneity of visual improvement as well as to decide the follow up interval appropriately [2].

Nowadays, the clinical trials have been mentioned the potential achieving of intravitreal anti-VEGF agents for treatment visual impairment of macular edema secondary to central retinal vein occlusion (CRVO) [3-6]. Corticosteroids have been used orally or intravitreally in CRVO to stabilize retinal vessel tight junctions and reduce macular edema by indirect anti-vascular endothelial growth factor (VEGF) action of corticosteroid [7, 8]

There are several population-based studies mentioned about Caucasian populations in the prevalence study which provides valuable information related to systemic risk factors of RVO. Risk factors include hypertension, diabetes, smoking habits, dyslipidemia and a history of angina [9-14].

2. Methods

This study was designed as a retrospective study of central retinal vein occlusion in younger and older patients at Thammasat Eye Hospital from 1st January 2017 to 31st December 2018. This study was approved by The Human Ethics Committee of Thammasat University with declaration of Helsinki number 243/2020. The patients were selected from 78

patients of Central Retinal Vein Occlusion who were diagnosed in the period of study. 10 patients were excluded from study due to 3 patients were unknown the clinical onset and 7 patients were incomplete documents. As a result, 68 patients were enrolled in this study and divided into two age groups: < 50 years and ≥ 50 years at CRVO onset.

Inclusion criteria were: a complete history taking including duration of CRVO first occurred, gender, laterality of the eye, and smoking status as well as concurrent diagnoses of hypertension, diabetes mellitus, hyperlipidemia, and glaucoma. The initial eye presentation was included for analysis for those patients who later developed a subsequent CRVO in the fellow eye. Exclusion criteria included: unknown the duration of CRVO onset, other retinopathies mimicking CRVO, and patients with inadequate information.

Ophthalmological examination at initial presentation included duration of symptoms before diagnosis, previous treatments, characterization of perfusion status of CRVO as ischemic or nonischemic, best corrected visual acuity, intraocular pressure (IOP), lens status, presence of relative afferent pupillary defect, neovascularization of the iris, angle, optic disc, or elsewhere, and vitreous hemorrhage. Spectral domain optical coherence tomography images were reviewed for presence of cystoid macular edema (CME), subretinal fluid (SRF), central subfield thickness (CST). A CRVO was characterized by the presence of venous dilation and tortuosity, retinal hemorrhage with or without cotton wool spot and/or optic disc edema. Each CRVO was classified as ischemic or nonischemic. CRVO was defined as ischemic if there was either evidence of and neovascular sequelae attributable to the CRVO or presence of count fingers vision or worse (due to the CRVO) with a concurrent afferent pupillary defect confirmed by ophthalmologists. Visual acuity

was assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, and vision categories were defined according to ETDRS scoring standards [15]. Conversion of Snellen Equivalents to LogMAR was used followed by [16]. The final examination available for the affected eye was reviewed to calculate the number of months from onset to final follow-up, number of CRVO-related treatments, and those same clinical parameters that were recorded from the initial visit.

Treatments were defined as intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents (bevacizumab, ranibizumab, and aflibercept) and intravitreal or periocular steroids. Documentation of gonioscopy and performance of pan-retinal photocoagulation were also recorded. The electronic medical record of each younger patient was reviewed for systemic health diagnoses and factors that may potentially be contributed to CRVO development. All statistical data were analyzed using an IBM SPSS version 23 and recorded using Microsoft Excel 2013. Paired student's t-test was used to compare baseline and final visual acuity data. A *p*-value of less than 0.05 was considered to be significant.

3. Results

Among 68 central retinal vein occlusion patients, 29 women and 39 men met the inclusion criteria. 15 patients (22.05%) were younger than 50 years old and 53 patients (77.94%) were equal to or older than 50 years old. Demographic data of the study patients is reported in Table 1. Patients were diagnosed as non-ischemic (*n* = 43), ischemic (*n* = 22) and unidentified (*n* = 3). The total mean age was 59.5 ± 14.05 years old, ranging from 18 - 88 years old. The mean onset of the symptoms of the disease was 32.44 ± 40.9 days. The mean follow-up of total patients was 19.04 ± 5.68 months with 19.07 ± 6.18 in young adults and 19.03 ± 5.60 in older patients. All patients had at least 9 months of follow-up. CRVO occurred in the left eye in 32 patients (47.06%), in the right eye 36 patients (52.94%). 2 patients developed CRVO in the fellow eye during the follow-up period.

Table 1: Demographic data for patient CRVO

Patients	<50 y n (%) 15 (22)	≥50Y n (%) 53 (78)	Total n (%) 68 (100%)
Gender, n (%)			
Women	7 (46.67)	22 (41.5)	29 (42.65)
Man	8 (53.33)	31 (58.5)	39 (57.35)
Age (year), Mean ± SD	39.4 ± 9.27	65.11 ± 9.45	59.44 ± 14.23
Onset (day)	26.76 ± 31.68	34.24 ± 43.72	32.44 ± 40.9
Laterality, n (%)			
Left	8 (53.33)	24 (45.28)	32 (47.06)
Right	7 (46.67)	29 (54.72)	36 (52.94)
Mean follow-up (month)	19.07 ± 6.18	19.03 ± 5.60	19.04 ± 5.68
Hypertension, n (%)	8 (53.33)	36 (68)	44 (64.71)
Diabetic, n (%)	2 (13.33)	24 (45.28)	26 (38.24)
Hyperlipidemia, n (%)	7 (46.67)	25 (47.17)	32 (47.06)

Glaucoma, n (%)	0	6 (11.32)	6 (8.82)
Active Smoker, n (%)	2 (13.33)	0	0
Retinal vein occlusion type, n (%)			
Nonischemic	12(80)	31 (58.49)	43 (63.24)
Ischemic	2 (13.33)	20(37.74)	22 (32.35)
Unknown	1 (6.67)	2(3.77)	3 (4.41)

4. Risk Factors

Of the 15 younger patients in this study, 8 (53.33%) had hypertension, 7 (46.67%) had hyperlipidemia, 2 (13.33%) had diabetes, 2 (13.33%) were active smokers and none of patients presented with glaucoma history (Table 1). All younger patients were enrolled for clinical work-up and laboratory test for non-traditional risk factors, antinuclear antibody, lupus anticoagulant, homocysteine level and a coagulant factor test including platelet, antithrombin III activity, activated partial thromboplastin time, fibrinogen, protein C activity, plasminogen activity. 9 (60%) younger patients were identified with non-traditional risk factors. 2 patients were reported with lupus anticoagulant test positive. 1 patient had antinuclear antibody and antithrombin III activity positive. 1 patient had antithrombin III activity positive. 1 woman were on hormonal oral contraceptive, history of gestational diabetes mellitus and on treatment of Ventolin by Asthma disease. A result of work up in younger patients showed that 1 patient was found a cerebrovascular accident. 1 patient had chronic kidney disease. 1 patient had chronic obstruction pulmonary, whereas another had asthma.

Of the 53 older patients in this study, 36 (68%) had hypertension, 25 (47.17%) had hyperlipidemia, 24 (45.28%) had diabetes, and 6 (11.32%) had a history of glaucoma. One older patient was presented with corona artery disease, one patient had chronic kidney disease, one patient had obstruction sleep apnea and another one had stroke during the follow up. Associated systemic conditions of CRVO patients in both groups were treated.

5. Visual Outcome

According to table 2, the mean baseline visual acuity of the affected eyes was 1.13 ± 0.61 logMAR (range 0 - 3 logMAR). At baseline, the mean VA was 1.02 ± 0.73 logMAR in younger patients and 1.16 ± 0.57 logMAR in older patients. At the final follow-up, the overall mean visual acuity improved to 0.87 ± 0.58 logMAR. The final mean VA was 0.52 ± 0.61 logMAR in younger patients and 0.97 ± 0.54 logMAR in older patients. Compared with baseline, the improvement in VA was statistically significant in both age groups with *p*-value of 0.002.

The mean baseline VA of fellow eye was 0.29 ± 0.32 logMAR (range 0 - 1.3 logMAR). Baseline mean VA was 0.11 ± 0.15 logMAR in younger patients and 0.34 ± 0.33 logMAR in older patients. At the final follow-up, the mean VA of the fellow eye was 0.24 ± 0.22 logMAR. The mean visual acuity at the final follow-up of young and old adult was 0.04 ± 0.11 logMAR and

0.30 ± 0.21 logMAR respectively. There is no statistically significant change in fellow-eye VA was observed in either age group ($p = 0.10$ and $p = 0.20$, respectively).

At the final follow-up, subgroup analysis demonstrated no statistically significant improvement in final VA among female patients, patient's onset of symptom > 30 days, pseudophakic patients and patients with baseline CFT ≤ 300 μm . In contrast, significant improvement in VA was observed in male patients and in those who received treatment within 30 days of symptom onset (both $p < 0.0001$). Significant visual improvement was also observed in phakic patients, non-ischemic CRVO, ischemic CRVO, and patients with baseline CFT > 300 μm ($p < 0.0001$, $p = 0.002$, $p = 0.0001$ and $p < 0.0001$ respectively). The proportion of ischemic CRVO was higher in older than in younger patients (37.74% vs. 13.33%).

Table 2: Visual acuity outcome

	Visual Acuity (log MAR) <i>p-value</i>	
	Initial VA	Final VA
All participants of patient's eye	1.13 ± 0.61	0.87 ± 0.58
Patient Eye (young adult)	1.02 ± 0.73	0.52 ± 0.61 <i>0.002</i>
Patient Eye (old adult)	1.16 ± 0.57	0.97 ± 0.54 <i>0.002</i>
All participants of fellow eye	0.29 ± 0.32	0.24 ± 0.22
Fellow Eye (young adult)	0.11 ± 0.15	0.04 ± 0.11 <i>0.10</i>
Fellow Eye (old adult)	0.34 ± 0.33	0.30 ± 0.21 <i>0.20</i>
Male	1.13 ± 0.56	0.8 ± 0.49 <i>< 0.0001</i>
Female	1.13 ± 0.68	0.97 ± 0.68 <i>0.07</i>
Onset 1-30 days	1.11 ± 0.62	0.81 ± 0.59 <i>< 0.0001</i>
Onset > 30 days	1.03 ± 0.45	0.84 ± 0.51 <i>0.17</i>
Phakic	1.15 ± 0.61	0.87 ± 0.58 <i>< 0.0001</i>
Pseudophakic	1 ± 0.64	0.92 ± 0.63 <i>0.18</i>
Non-ischemic	0.35 ± 0.35	0.7 ± 0.2 <i>0.002</i>
Ischemic	1.78 ± 0.37	1.37 ± 0.48 <i>0.0001</i>
CFT ≤ 300 μm	1.16 ± 0.87	1.04 ± 0.72 <i>0.21</i>
CFT > 300 μm	1.15 ± 0.52	0.83 ± 0.53 <i>< 0.0001</i>

VA: Visual acuity, CFT: Central Foveal Thickness, μm : Micrometers

At the final follow up, the proportion of patients who gained ≥ 3 lines in BCVA was 46.66 % in younger adults and 47.17% in older adults (Table 3). No visual loss was observed in the younger group; however, in the older group, 24.52% experienced a loss of ≥ 1 line. The percentage of patients who achieved BCVA ≤ 0.3 logMAR at the final follow-up was 53.33% in younger adults and 13.2% in older adults (Table 3). At the final follow-up, one younger patient had a visual acuity

of hand motion due to macular thinning (OCT macular thickness 77 μm) secondary to retinal ischemia.

Table 3: Visual acuity of young and old patients

Visual acuity (logMAR)	Age < 50 y	Age ≥ 50 y
VA gain ≥ 3 lines	7 (46.66 %)	25 (47.17%)
VA gain 2 lines	3(20 %)	4 (7.54%)
VA gain 1 line	1 (6%)	3 (5.56%)
VA stable	4 (26.66%)	8 (15.09%)
VA loss ≥ 1 line	0	13 (24.52%)
Final VA		
VA ≤ 0.3	8 (53.33%)	7 (13.2%)
VA 0.4 – 0.7	4 (26.66%)	13 (24.52%)
VA 0.8 – 1.10	0	15 (28.30%)
VA ≥ 1.2	3 (20%)	18 (33.96%)

Complications observed in this study included persistent macular edema, vitreous hemorrhage and neovascular glaucoma (Table 4). Macular edema and vitreous hemorrhage were the most common causes of decreased in visual acuity during follow up. Vitreous hemorrhage occurred in 12 of 68 patients (17.64%). All of vitreous hemorrhage patients had final visual acuity worse than 1 logMAR and one patient was reported with none clearing vitreous hemorrhage and subsequently underwent pars plana vitrectomy.

Table 4. Ocular Complications of central retinal vein occlusion

	< 50 y (N=15)	≥ 50 y (N=53)	Total (N=68)
Macular Edema	9 (60)	45 (84.91)	54 (79.41)
Vitreous Hemorrhage	1(6.67)	11(20.75)	12 (17.65)
Neovascularization, n (%)	3 (20)	20(37.74)	23 (33.82)
Iris	0	1 (1.89)	1 (1.47)
Angle	0	4(7.55)	4 (5.88)
Disc	2(13.33)	4(7.55)	6 (8.82)
Elsewhere	1(6.67)	11(20.75)	12 (17.65)

The mean baseline central subfield thickness (CST) of the affected eyes was 449.56 ± 176.48 μm compared with 251.62 ± 34.40 μm in the fellow eyes. The final mean of CST was 339.72 ± 145.68 μm in the affected eyes and 243.49 ± 38.64 μm in the fellow eyes (Table 5).

Table 5: Comparison between baseline and final follow-up of central subfield thickness

	Younger (< 50 y)	Older (≥ 50 y)	Total
Baseline (CST (μm), Mean $\pm$ SD)			
Presenting eye	372.15 ± 142.54	470.1 ± 180.13	499.56 ± 176.48
Fellow eye	241.23 ± 15.28	254.43 ± 37.59	251.62 ± 34.40
Final Follow-up (CST (μm), Mean $\pm$ SD)			
Presenting eye	239.44 ± 46.41	359.34 ± 150.6	339.72 ± 145.68
Fellow eye	240.66 ± 10.67	244.09 ± 42.38	243.49 ± 38.64

Medical treatment was performed in 62 patients (91.17%), including 11 younger patients (73.33%) and 51 older patients (96.23%). There was no treatment in four younger patients because three of these patients had no macular edema and another one had mild extra-foveal edema. In older patients' group, only 2 patients had no treatment. One patient refused to accept the treatment and another one had no macular edema. Treatment included intravitreal injection of anti-VEGF agent

(Bevacizumab, Ranibizumab or Aflibercept) for macular edema and pan-retinal photocoagulation in the presence of neovascularization. None of patient was documented to receive intravitreal steroid.

Younger patients received fewer intravitreal injections of any type (3.72 ± 3.16) compared with older patients (5.54 ± 3.13) over the mean duration of follow-up (19.07 ± 6.08 vs 19.03 ± 5.60). The younger group also received fewer laser treatment (pan-retinal photocoagulation) than the older group (13.33% vs 22.64%) (Table 6).

Table 6: Treatments administered during follow-up

	< 50y (N=15)	≥50y (N=53)	Total (N=68)
Treatment	11 (73.33)	51 (96.23)	62 (91.17)
Pan-retinal photocoagulation	1 (6.67)	12 (22.64)	13 (19.12)
Mean number of Intravitreal injections $\pm$ SD			
Bevacizumab	2.33 $\pm$ 1.75	3.26 $\pm$ 2.26	3.09 $\pm$ 2.17
Ranibizumab	4.8 $\pm$ 3.89	3.39 $\pm$ 2.04	3.5 $\pm$ 2.3
Aflibercept	2	4.21 $\pm$ 2.5	4.1 $\pm$ 2.48

6. Discussion

The purpose of this study was to identify the predictive factors of visual prognosis in younger and older patients of Central Retinal Vein Occlusion. Our study shows that systemic hypertension was the most common risk factor in both age groups, consistent with previous reports [17, 24-27]. Peripheral vein disease and peripheral artery disease were also identified as significant risk factors. Previous studies reported that 11.4% - 19.8% of patients with CRVO were less than 50 years old of age, Rothman et al [17] reported 36 of 269 patients (13%), Quinlan et al [18] 24 of 160 (15%); Brown et al [19] 4 of 35 (11.4%); Kohner and Cappin [20] 23 of 116 (19.8%). Similarly, our results show that 22% of patients were younger or equal to 50 years old of age. Younger patients had better baseline and final visual acuity compared with older patients. Previous research has demonstrated that retinal ischemia is a reliable predictor of both presenting and final visual acuity in younger patients [21-23]. Rothman et al. [17] further noted that younger patients had a lower incidence of CME, thinner CST at presentation, and required fewer treatments over time.

The CRUISE study [28] mentioned that treatment benefits were greatest when CRVO duration was less than 3 months at screening. Patients with worse baseline BCVA and CFT >450 μ m showed greater mean BCVA improvement at 6 months. Similarly, our study found significant visual acuity improvement in male patients, those presenting within 30 days of symptom onset, phakic patients, and both non-ischemic and ischemic CRVO (Table 5). Consistent with previous anti-VEGF trials, earlier treatment was associated with better visual outcomes, whereas delayed treatment resulted in smaller visual gains. Younger patients were also more likely to achieve a final visual acuity of ≤ 0.3 logMAR than older patients, and none experienced visual deterioration. However, final visual acuity

remained poor in ischemic CRVO regardless of age or treatment.

In our cohort study, 90.47% of patients with ischemic CRVO presenting with the initial visual acuity of 1 logMAR or worse remained poor visual acuity in the final visit, aligns with previous studies [29,30]. Severe visual impairment is strongly associated non-perfused CRVO [29]. Therefore, the primary concern should be the prevention of neovascular glaucoma and prompt treatment should be done if new vessels develop.

This study has several limitations. Its retrospective design which resulted in missing data such as fundus fluorescein angiography to confirm non-perfusion areas. Additionally, the absence of a control group limits the ability to assess treatment benefit. Patients were managed by different physicians, which may have introduced variability in workup or treatment protocols; although all patients with CRVO received standard of care, there may have been differences in imaging obtained at various visits, intervention protocol, follow-up intervals, and other factors.

In conclusion, visual prognosis in patients with central retinal vein occlusion is strongly influenced by disease subtype. Non-ischemic CRVO is associated with more favorable visual outcomes, whereas ischemic CRVO generally has poorer prognosis despite treatment. Younger age, treatment initiated within 30 days of symptom onset, and male sex were associated with better final visual acuity. Early diagnosis and prompt treatment may improve visual outcomes and reduce disease-related complications.

References

- [1] Laouri M, Chen E, Looman M, Gallagher M. The burden of disease of retinal vein occlusion: review of the literature. *Eye (Lond)*. 2011;25(8):981-988.
- [2] Prajna NV. Aravind FAQs in Ophthalmology. New Delhi: Jaypee Brothers Medical Publishers; 2018.
- [3] Boyer D, Heier J, Brown DM, Clark WL, Vitti R, Berliner AJ, et al. Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase III COPERNICUS study. *Ophthalmology*. 2012;119(5):1024-1032.
- [4] Brown DM, Heier JS, Clark WL, Boyer DS, Vitti R, Berliner AJ, et al. Intravitreal aflibercept injection for macular edema secondary to central retinal vein occlusion: 1-year results from the phase 3 COPERNICUS study. *Am J Ophthalmol*. 2013;155(3):429-437.e7.
- [5] Holz FG, Roider J, Ogura Y, Korobelnik JF, Simader C, Groetzsch G, et al. VEGF Trap-Eye for macular oedema secondary to central retinal vein occlusion: 6-month results of the phase III GALILEO study. *Br J Ophthalmol*. 2013;97(3):278-284.
- [6] Brown DM, Campochiaro PA, Singh RP, Li Z, Gray S, Saroj N, et al. Ranibizumab for macular edema following central retinal vein occlusion: six-month primary end

- point results of a phase III study. *Ophthalmology*. 2010;117(6):1124-1133.e1.
- [7] Hayreh SS. Venous occlusive disease: management 25 years ago. *Retina*. 2006;26(6 Suppl):S51-S62.
 - [8] Gregori NZ, Scott IU, Berrocal AM, Murray TG, Smiddy WE, Mavroufides EC, et al. One-year safety and efficacy of intravitreal triamcinolone acetonide for the management of macular edema secondary to central retinal vein occlusion. *Retina*. 2006;26(8):889-895.
 - [9] Wong TY, Larsen EKM, Klein R, Mitchell P, Couper DJ, Klein BE, et al. Cardiovascular risk factors for retinal vein occlusion and arteriolar emboli: the Atherosclerosis Risk in Communities and Cardiovascular Health Studies. *Ophthalmology*. 2005;112(4):540-547.
 - [10] Cheung N, Klein R, Wang JJ, Cotch MF, Islam AF, Klein BE, et al. Traditional and novel cardiovascular risk factors for retinal vein occlusion: the Multi-Ethnic Study of Atherosclerosis. *Invest Ophthalmol Vis Sci*. 2008;49(10):4297-4302.
 - [11] Cugati S, Wang JJ, Rochtchina E, Mitchell P. Ten-year incidence of retinal vein occlusion in an older population: the Blue Mountains Eye Study. *Arch Ophthalmol*. 2006;124(5):726-732.
 - [12] Lim LL, Cheung N, Wang JJ, Islam FM, Mitchell P, Saw SM, et al. Prevalence and risk factors of retinal vein occlusion in an Asian population. *Br J Ophthalmol*. 2008;92(10):1316-1319.
 - [13] Klein R, Klein BEK, Moss SE, Meuer SM. The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study. *Trans Am Ophthalmol Soc*. 2000;98:133-141.
 - [14] Kawasaki R, Wong TY, Wang JJ, Kayama T, Yamashita H. Body mass index and vein occlusion. *Ophthalmology*. 2008;115(5):917-918.
 - [15] Kaiser PK. Prospective evaluation of visual acuity assessment: a comparison of Snellen versus ETDRS charts in clinical practice (an AOS thesis). *Trans Am Ophthalmol Soc*. 2009;107:311-324.
 - [16] Tripathy K, Gupta A. Evaluation of visual acuity. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [updated 2024 May 1]. PMID: 33231977.
 - [17] Rothman AL, Thomas AS, Khan K, Fekrat S. Central retinal vein occlusion in young individuals: a comparison of risk factors and clinical outcomes. *Retina*. 2019;39(10):1917-1924.
 - [18] Quinlan PM, Elman MJ, Bhatt AK, Mardesich P, Enger C. The natural course of central retinal vein occlusion. *Am J Ophthalmol*. 1990;110(2):118-123.
 - [19] Brown GC, Shah HG, Magargal LE, Savino PJ. Central retinal vein obstruction and carotid artery disease. *Ophthalmology*. 1984;91(12):1627-1633.
 - [20] Kohner EM, Cappin JM. Do medical conditions have an influence on central retinal vein occlusions? *Proc R Soc Med*. 1974;67(10):1052-1054.
 - [21] Johnson RN, Nadel A, Zegarra H, Joffe L, Maberley AL, Burton T, et al. Central retinal vein occlusion in young adults (papillophlebitis). *Retina*. 1992;12(1):3-11.
 - [22] Hayreh SS, Podhajsky PA, Zimmerman MB. Natural history of visual outcome in central retinal vein occlusion. *Ophthalmology*. 2011;118(1):119-133.e2.
 - [23] Magargal LE, Gonder JR, Maher V. Central retinal vein obstruction in the young adult. *Trans Pa Acad Ophthalmol Otolaryngol*. 1985;37(2):148-153.
 - [24] Bertelsen M, Linneberg A, Christoffersen N, Vorum H, Gade E, Larsen M. Mortality in patients with central retinal vein occlusion. *Ophthalmology*. 2014;121(3):637-642.
 - [25] Rath EZ, Frank RN, Shin DH, Kim C. Risk factors for retinal vein occlusions: a case-control study. *Ophthalmology*. 1992;99(4):509-514.
 - [26] The Eye Disease Case-Control Study Group. Risk factors for central retinal vein occlusion. *Arch Ophthalmol*. 1996;114(5):545-554.
 - [27] Haller JA, Bandello F, Belfort R Jr, Blumenkranz MS, Gillies M, Heier J, et al. Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion: twelve-month study results. *Ophthalmology*. 2011;118(12):2453-2460.
 - [28] Lu S, Nguyen C, Patel A. Central retinal vein occlusion: a review of current evidence-based treatment options. *Middle East Afr J Ophthalmol*. 2016;23(1):44-48.
 - [29] The Central Vein Occlusion Study Group. Natural history and clinical management of central retinal vein occlusion. *Arch Ophthalmol*. 1997;115(4):486-491.
 - [30] The Central Vein Occlusion Study Group. A randomized clinical trial of early panretinal photocoagulation for ischemic central vein occlusion. *Ophthalmology*. 1995;102(10):1434-1444.