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CLINICAL CHARACTERISTICS OF PATIENTS WITH RETINAL VEIN OCCLUSION AND MACULAR EDEMA AT CIPTO MANGUNKUSUMO HOSPITAL KIRANA IN INDONESIA

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Abstract

***Introduction**: Retinal vein occlusion (RVO) is a significant retinal vascular disease, often resulting in macular edema and vision impairment. This study aims to investigate the clinical characteristics, management, and outcomes of RVO patients with macular edema at Cipto Mangunkusumo Hospital Kirana from January 2020 to December 2021.*

***Methods**: This retrospective descriptive study analyzed medical records of 85 RVO patients with macular edema. Demographic data, clinical characteristics, management approaches, and treatment outcomes were examined. Data were analyzed using SPSS.*

***Results**: Most patients were over 50 years old, predominantly male, and affected in one eye. Hypertension and diabetes mellitus were common comorbidities. Central RVO cases had worse initial visual acuity and macular thickness than branch RVO cases. Anti-VEGF injections were the primary therapy, and patients received an average of two injections in the first year. Macular thickness reduced after anti-VEGF injections, but visual acuity improvement was minimal.*

***Conclusion**: Patients with RVO and macular edema are often older males with systemic risk factors. Anti-VEGF injections are the primary treatment, with improvements in macular thickness but limited visual acuity gain. Patient education, comprehensive management, and public awareness are recommended to enhance RVO care. Further research to analyze parameter relationships is needed.*

Keywords: Retinal vein occlusion, macular edema, anti-VEGF injections, visual acuity, demographic characteristics.

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INTRODUCTION

Retinal vein occlusion (RVO) is the second most common retinal vascular disease after diabetic retinopathy. Retinal vein occlusion occurs due to the presence of a thrombus that can block any part of the retinal vein. Based on the location of the obstruction, RVO can be classified into central retinal vein occlusion, branch retinal vein occlusion, or hemispheric retinal vein occlusion.[1] Additionally, RVO can be categorized as ischemic or non-ischemic.[2] Risk factors for RVO include old age, hypertension, smoking, open-angle glaucoma, diabetes mellitus, hyperlipidemia, hypercoagulopathy, and hyperthyroidism.[1]

The pathogenesis of retinal vein occlusion follows Virchow's triad for thrombosis pathogenesis, which includes vascular endothelial damage, venous stasis, and hypercoagulability.[1,3] At the cellular level, retinal ischemia resulting from disrupted retinal circulation leads to local regulatory increases, the release of vascular endothelial growth factor (VEGF), and various inflammatory mediators into the retina. The release of VEGF into the retina causes macular edema and neovascularization.[1]

In 2015, the prevalence of RVO was 0.77%, with branch RVO accounting for 0.64% and central RVO for 0.13%.[4] Research conducted by Putera I at Cipto Mangunkusumo Hospital (RSCM) found that in 2018, 61% of RVO cases out of 97 new cases were branch RVO.[5] This figure increased compared to previous research by Diana N, where over three years from 2011 to 2013, there were only 88 new cases of branch RVO.[6] Macular edema is the most common complication of RVO that results in decreased visual acuity.[7,8]

Management of macular edema in RVO includes photocoagulation laser treatment, intravitreal steroids, intravitreal anti-VEGF drugs, or vitrectomy surgery.[9,11,12] Despite various therapies available for managing macular edema in RVO, 31-56% of cases may experience recurrent or persistent macular edema.[13]

The study conducted by Putera in 2018 at RSCM indicated a higher incidence of edema occurrence in branch retinal vein occlusion (BRVO) compared to central retinal vein occlusion (CRVO). However, this data solely addressed the incidence of macular edema in RVO, without elaborating on therapy types and outcomes. Thus, the current research aims to obtain information pertaining to the number of patients, demographic and clinical characteristics, management approaches, and management outcomes for RVO patients with macular edema at RSCM. The general objectives of this study is to acquire information regarding the patient count, demographic characteristics, clinical profile, management strategies, and treatment outcomes of retinal vein occlusion (RVO) patients with macular edema at RSCM Kirana during the period of January 2020 to December 2021.

METHODS

This retrospective descriptive study was conducted at Cipto Mangunkusumo Hospital in Jakarta during the research period spanning from May to June 2023. This research has been declared ethically reviewed by the Health Research Ethics Committee of FKUI-RSCM with the number KET-663/UN2.F1/ETIK/PPM.00.02/2023 on May 29, 2023. The study drew upon medical record data collected from January 2020 to December 2021, with a focus on patients at RSCM Kirana who experienced retinal vein occlusion (RVO) accompanied by macular

edema within this timeframe. Study subjects were selected based on specific inclusion and exclusion criteria, ensuring the research's relevance to the targeted population. The data extracted from medical records were meticulously organized into an index table for subsequent analysis. These variables were then subjected to statistical analysis using SPSS version 23.0 (SPSS Inc., Chicago, Illinois). Numeric variables were represented as means and standard deviations when data distribution followed a normal pattern, while medians (minimum-maximum) were employed for variables with non-normal distributions. Categorical data were presented as proportions, providing a comprehensive overview of the study's findings.

Table 1. Demographic characteristics of RVO patients with macular edema

Variable(n=85)	OVRS, n(%)	OVRC, n(%)	Total, n(%)
Age			
(median [min-max])	55.2 (16-81)	60.0 (38-72)	57.4 (16-81)
Gender			
Man	29 (56.9%)	22 (64.7%)	51 (60.0%)
Women	22 (43.1%)	12 (35.3%)	34 (40.0%)
Laterality			
Unilateral	44 (86.3%)	33 (97.1%)	77 (90.6%)
Bilateral	7 (13.7%)	1 (2.9%)	8 (9.4%)

RESULTS

From patient data collected through medical records from January 2020 to December 2021, a total of 85 patients with a diagnosis of retinal vein occlusion (RVO) accompanied by macular edema were identified. The number of central retinal vein occlusion (CRVO) cases (OVRS) was 51, and the number of branch retinal vein occlusion (BRVO) cases (OVRC) was 34.

Demographic Characteristics of RVO Patients with Macular Edema

In this study, based on the analysis of patient demographic characteristics in Table 1, the median age of RVO patients with macular edema was found to be 57.4 (16-81) years. The patient population was predominantly male, both in cases of CRVO and BRVO, with a total of 60.0% male patients. The majority of cases involved only one eye, but in 13.7% of CRVO cases and 2.9% of BRVO cases, involvement in both eyes was observed.

Table 2. Clinical Characteristics of RVO Patients with Macular Edema

Variable (n=85)	OVRS, n(%)	OVRC, n(%)	Total, n(%)
Clinical manifestation's duration			
≤ 1 week	6 (11.8%)	2 (5.9%)	8 (9.4%)
>1 week - 1 month	21 (41.2%)	13 (38.2%)	34 (40.0%)
>1 - 2 months	8 (15.7%)	8 (23.5%)	16 (18.8%)
>2 - 6 months	14 (27.5%)	7 (20.6%)	21 (24.7%)
> 6 months	2 (3.9%)	4 (11.8%)	6 (7.1%)
Initial visual acuity			
≥ 6/12 (LogMAR ≥ 0,30)	3 (5.9%)	9 (26.5%)	12 (14.1%)
< 6/12 s.d. ≥ 6/18 (LogMAR < 0,30 s.d. ≥ 0,48)	2 (3.9%)	4 (11.8%)	6 (7.1%)
< 6/18 s.d.≥ 6/60 (LogMAR < 0,48 s.d. ≥1,00)	13 (25.5%)	14 (41.2%)	27 (31.8%)
< 6/60 s.d. ≥ 3/60 (LogMAR < 1,00 s.d. ≥1,30)	1 (2.0%)	1 (2.9%)	2 (2.4%)
< 3/60 (LogMAR < 1,30)	32 (62.7%)	6 (17.6%)	38 (44.7%)
Lens status			
Phakia	44 (86.3%)	30 (88.2%)	74 (87.1%)
Pseudophakia	6 (11.8%)	3 (8.8%)	9 (10.6%)
N/A	1 (2.0%)	1 (2.9%)	2 (2.4%)
Initial thickness of macula, µm	559.0 (275-	424.0 (277-984)	513.0 (275-
(median [min-max])	1799)		1799)
Initial IOP, mmHg			
(median [min-max])	13.0 (8-54)	11.0 (6-22)	12.0 (6-54)
Comorbid conditions			
Hypertension	35 (68.6%)	25 (73.5%)	60 (70.6%)
Diabetes mellitus	16 (31.4%)	7 (20.6%)	23 (27.1%)
Heart conditions	4 (7.8%)	1 (2.9%)	5 (5.9%)
Dyslipidemia	1 (2.0%)	4 (11.8%)	5 (5.9%)
Stroke	3 (5.9%)	1 (2.9%)	4 (4.7%)
Injection count			
(median [min-max])	2.0 (1-10)	2.0 (1-7)	2.0 (1-10)

Clinical Characteristics of RVO Patients with Macular Edema

In Table 3.2, the duration of complaints in RVO cases with macular edema varied from less than 1 week to over 6 months, with the highest duration falling within the range of more than 1 week to 1 month (Total 40.0%; OVRS 41.2%, OVRC 38.2%).

In cases of CRVO, the highest visual acuity observed was < 3/60 (LogMAR < 1.30), while in cases of BRVO, it ranged from < 6/18 to ≥ 6/60 (LogMAR < 0.48 to ≥ 1.00). The majority of patients had phakic lens status (87.1%), with a median initial macular thickness of 513.0 (275-1799) µm and initial intraocular pressure (IOP) of 12.0 (6-54) mmHg. The total number of injections had a median of 2.0 (1-10) times.

Management of RVO with Macular Edema

Various types of interventions and combinations were employed for managing RVO with macular edema, with the most common approach being anti-VEGF injections at 62.5% (Table 3)

Table 3. Management of RVO with Macular Edema

Variety of management (n=48)	OVRS, n(%)	OVRC, n(%)	Total, n(%)	Komplikasi tindakan, n(%)
Intravitreal Anti-VEGF Injection	20 (62.5%)	10 (62.5%)	30 (62.5%)	0 (0.0%)
Combination of Intravitreal Anti-VEGF Injection + Laser Photocoagulation	7 (21.9%)	3 (18.8%)	10 (20.8%)	0 (0.0%)
Combination of Intravitreal Anti-VEGF Injection + Steroid	1 (3.1%)	1 (6.2%)	2 (4.2%)	0 (0.0%)
Combination of Intravitreal Anti-VEGF Injection + Steroid + Laser Photocoagulation	2 (6.2%)	0 (0.0%)	2 (4.2%)	0 (0.0%)
Combination of Intravitreal Anti-VEGF Injection + Vitrectomy	1 (3.1%)	0 (0.0%)	1 (2.1%)	1 (100.0%)*
Combination of Laser Photocoagulation + Vitrectomy Without ILM Peeling + Combination of Intravitreal Anti-VEGF Injection + Steroid + Vitrectomy + Phacoemulsification	1 (3.1%)	1 (2.1%)	2 (4.2%)	0 (0.0%)
Non-Steroidal Anti-Inflammatory Drug (NSAID) Eye Drops	0 (0.0%)	1 (6.2%)	1 (2.1%)	0 (0.0%)

In CRVO cases (OVRS), the management pursued by patients included anti-VEGF injections (62.5%), a combination of anti-VEGF injections and photocoagulation laser (21.9%), a combination of anti-VEGF injections and steroids (3.1%), a combination of anti-VEGF injections + steroids + photocoagulation laser (6.2%), a combination of anti-VEGF injections and vitrectomy (3.1%), and a combination of photocoagulation laser and vitrectomy without ILM peeling (3.1%).

Meanwhile, in BRVO cases (OVRC), the interventions consisted of anti-VEGF injections (62.5%), a combination of anti-VEGF injections and photocoagulation laser (18.8%), a combination of anti-VEGF injections and steroids (6.2%), and a combination of anti-VEGF + steroids + vitrectomy + phacoemulsification, accounting for 6.2% of cases. One individual in the BRVO group received only conservative therapy with topical NSAID eye drops.

Complications of the interventions were observed in only 1 case, involving vitreous hemorrhage following VEGF injection, which subsequently necessitated vitrectomy surgery.

Analysis of Changes in Central Macular Thickness at the Beginning and End of Treatment

Based on macular thickness measurements, cases of CRVO generally exhibited thicker macular layers compared to BRVO cases, both before and after therapy. When assessing the difference between initial and final macular thickness, for cases treated with anti-VEGF injections, the median decrease in macular thickness was 226.5 ([-933]-274) µm for OVRS and 165.0 ([-467]-[-20]) µm for OVRC. For cases treated with a combination of anti-VEGF injections and photocoagulation laser, the median decrease in macular thickness was 267.0 ([-1237]-90) µm for CRVO and 196.0 ([-411]-[-74]) µm for BRVO.

Table 4. Central macular thickness in CRVO with macular edema.

Variety of management (n=32)	Initial macular thickness [median (min-max)]	Final macular thickness [median (min-max)]	Δ Macular thickness [median (min-max)]
Intravitreal Anti-VEGF Injection	512.5 (275-1337)	279.5 (202-591)	-226.5 ([-933]-274)
Combination of Intravitreal Anti-VEGF Injection + Laser Photocoagulation	722.0 (328-1799)	455.0 (149-636)	-267.0 ([-1237]-90)
Combination of Intravitreal Anti-VEGF Injection + Steroid	544.0	240.0	-304.0
Combination of Intravitreal Anti-VEGF Injection + Steroid + Laser Photocoagulation	1180.5 (929-1432)	405.5 (199-612)	-775.0 ([-820]-[-730])
Combination of Intravitreal VEGF Injection + Vitrectomy	363.0	949.0	586.0
Combination of Laser Photocoagulation + Vitrectomy Without ILM Peeling	538.0	511.0	-27.0
Total	**554.5 (275-1799)**	**337.5 (149-949)**	**-233 ([-1237]-586)**

Interpretation: there's a decrease of central macular thickness after therapy in CRVO with macular edema patients.

Table 5.Central macular thickness in BRVO with macular edema.

Variety of management (n=16)	Initial macular thickness [median (min-max)]	Final macular thickness [median (min-max)]	Δ Macular thickness [median (min-max)]
Intravitreal Anti-VEGF Injection	409.0 (320-694)	261.0 (204-382)	-165.0 ([-467]-[-20])
Combination of Intravitreal Anti-VEGF Injection + Laser Photocoagulation	424.0 (313-644)	233.0 (228-239)	-196.0 ([-411]-[-74])
Combination of Intravitreal Anti-VEGF Injection + Steroid	513.0	173.0	-340.0
Combination of Intravitreal VEGF Injection + Steroid + Vitrectomy + Phacoemulsification	611.0	533.0	-78.0
Non-Steroidal Anti-Inflammatory Drug (NSAID) Eye Drops	436.0	321.0	-115.0
Total	**430.0 (313-694)**	**246.5 (173-533)**	**-158 ([-467]-[-20])**

Interpretation: there's a decrease of central macular thickness after therapy in BRVO with macular edema patients.

Analysis of Changes in Visual Acuity at the Beginning and End of Treatment

Based on visual acuity measurements, it is evident that visual acuity at the beginning and end of treatment generally improved more in OVRC compared to OVRS. Furthermore, there was an improvement in visual acuity after treatment for both OVRS and OVRC. In cases of OVRS, the median initial visual acuity was LogMAR 1.8 (0.1-2.3), and the final visual acuity was LogMAR 1.3 (0.0-3.0). Meanwhile, for OVRC, the median initial visual acuity was LogMAR 0.6 (0.0-2.3), and the final visual acuity was LogMAR 0.5 (0.0-1.8).

Table 6. Visual acuity in CRVO with macular edema.

Variety of management (n=32)	Initial visual acuity (Logmar) [median (min-max)]	Final visual acuity (Logmar) [median (min-max)]	Δ Logmar [median (min-max)]
Intravitreal Anti-VEGF Injection	1.6 (0.1-2.3)	1.3 (0.4-3.0)	0.0 ([-1.4]-1.9)
Combination of Intravitreal Anti-VEGF Injection + Laser Photocoagulation	1.8 (1.0-2.3)	1.3 (0.7-2.7)	0.0 ([-1.1]-0.5)
Combination of Intravitreal Anti-VEGF Injection + Steroid	0.6	0.0	-0.6
Combination of Intravitreal Anti-VEGF Injection + Steroid + Laser Photocoagulation	2.3	0.9	-1.4
Combination of Intravitreal VEGF Injection + Vitrectomy	0.7	3.0	2.3
Combination of Laser Photocoagulation + Vitrectomy Without ILM Peeling	0.3	2.3	2.0
Total	**1.8 (0.1-2.3)**	**1.3 (0.0-3.0)**	**0.0 ([-2.2]-2.3)**

Interpretation: there's a generally improved visual acuity after therapy in CRVO with macular edema patients.

Table 7. Visual acuity in BRVO with macular edema.

Variety of management (n=16)	Initial visual acuity (Logmar) [median (min-max)]	Final visual acuity (Logmar) [median (min-max)]	Δ Logmar [median (min-max)]
Intravitreal Anti-VEGF Injection	0.6 (0.0-1.8)	0.6 (0.0-1.8)	0.0 ([-0.5]-0.8)
Combination of Intravitreal Anti-VEGF Injection + Laser Photocoagulation	0.7 (0.2-1.8)	0.5 (0.5-1.8)	0.0 ([-0.2]-0.3)
Combination of Intravitreal Anti-VEGF Injection + Steroid	2.3	0.5	-1.8
Combination of Intravitreal VEGF Injection + Steroid + Vitrectomy + Phacoemulsification	0.3	0.7	0.4
Non-Steroidal Anti-Inflammatory Drug (NSAID) Eye Drops	0.3	0.3	0.0
Total	**0.6 (0.0-2.3)**	**0.5 (0.0-1.8)**	**0.0 ([-1.8]-0.8)**

Interpretation: there's a generally improved visual acuity after therapy in BRVO with macular edema patients.

DISCUSSION

OVR stands for retinal vein occlusion, involving either central retinal vein or its branches, which can cause changes in vision and long-term sequels.15Retinal vein occlusion occurs due to the presence of thrombus that can obstruct any part of the retinal vein. However, the causes of central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) differ based on their location. In CRVO, thrombus formation obstructs the central retinal vein near the lamina cribrosa. On the other hand, BRVO occurs when thrombus forms at the point of arteriovenous crossing due to retinal artery atherosclerosis, leading to compression of the retinal vein.15 Macular edema is one of the complications

of retinal vein occlusion and often becomes the cause of decreased vision in retinal vein occlusion cases.[7,8,10]

Risk factors for persistent macular edema in RVO include diabetes, type of RVO, time from diagnosis to treatment, early response to treatment, ischemia, increased baseline macular thickness, presence of cystoid macular edema, and loss of ellipsoid zone and external limiting membrane integrity.[12]

Demographic Characteristics of Patients with Macular Edema due to OVR

In this study, the occurrence of OVR, both CRVO and BRVO, was more common in males than females, with males accounting for 60% of OVR cases. This result is consistent with research by Thapa et al. and Ponto et al., indicating a higher prevalence of OVR in males than females.[16,17] Like other vascular diseases, male patients are more susceptible to OVR. In a study of 103 cases, Fong et al.[18] reported that 64% of patients were male. A study by Nalcaci in Turkey also found that 55% of OVR patients were male.19 Data from the IRIS Registry managed by the American Academy of Ophthalmology, which documents more than 1.2 million cases of retinal vascular occlusion in the United States, shows that the occurrence of CRVO is significantly higher in males, while BRVO occurs more frequently in females.[20] In the older population, cases in males are more common, possibly due to higher cardiovascular risk factors.

Based on age, the average age of patients in this study was over 50 years. The most significant factors in retinal vein occlusion are advanced age and systemic vascular diseases. According to IRIS Registry data, the proportion of retinal vascular occlusion cases increases with age: 0.5% of cases are under 25 years old, 2.7% are between 25 and 45 years old, and 24.3% are between 45 and 65 years old. Patients between 65 and 85 years old constitute the largest age group, accounting for 70.3% of cases.20 Hayreh et al.[21] found that 51% of retinal vein occlusion cases occurred in patients over 65 years old. The increasing occurrence with age may be attributed to higher cardiovascular risks in the elderly.[22]

Based on laterality, generally, both CRVO and BRVO cases involve a single eye more than both eyes, accounting for 90.6% of all cases, 86.3% of CRVO cases, and 97.1% of BRVO cases. This aligns with IRIS Registry data, which indicates that 90.5% of cases are unilateral.[20] Unilateral onset is more common than bilateral onset in all subtypes of retinal vascular occlusion. This unilateral onset is associated with the pathophysiology of vascular occlusion, both venous and arterial.

Clinical Characteristics of OVR with Macular Edema

Regarding comorbidities, several diseases were found in OVR cases. The most common comorbidity is hypertension, affecting 70.6% of cases, with an incidence of 68.6% in CRVO cases and 73.5% in BRVO cases. The second most frequent comorbidity is diabetes mellitus, with a total incidence of 27.1%, more commonly present in CRVO cases (31.4%) compared to BRVO cases (20.6%). Other comorbidities include dyslipidemia, heart disease, and stroke with lower incidence rates. These findings are consistent with previous studies reporting that retinal vein occlusion primarily occurs in the elderly and is associated with hypertension, diabetes, hyperlipidemia, cardiovascular disease, smoking, and open-angle glaucoma.[20,23] Among various risk factors, hypertension is the main risk factor for retinal vein occlusion. Studies in the UK and China assessed the impact of nine risk factors on the development of retinal vein occlusion, identifying hypertension as the greatest risk factor, followed by heart disease, stroke, elevated cholesterol, and increased creatinine.[4] The pathophysiology of retinal vein occlusion and hypertension is not fully understood, although several mechanisms have

been proposed.[23] Firstly, elevated blood pressure can directly damage retinal blood vessels, causing hemorrhage, cotton-wool spots, and macular edema. Secondly, systemic hypertension has been shown to affect ocular structures in various hypertensive eye disorders. For instance, systemic hypertension is associated with fewer perifoveal arterioles and venules and changes in retinal vascular structure. Chronic hypertension can also lead to arteriolar sclerosis, causing increased vascular resistance and decreased blood perfusion. Moreover, hypertension is associated with increased intraocular pressure and retinal microvascular abnormalities. Additionally, the renin-angiotensin-aldosterone system is known to be involved in the pathogenesis of ocular diseases.

Based on the initial visual acuity and macular thickness of patients with OVR in this study, there are differences in the degree of visual impairment and macular thickness between CRVO and BRVO. In CRVO cases, the highest proportion of visual acuity falls within the <3/60 or LogMAR <1.30 group, accounting for 62.7%, followed by the group with visual acuity <6/18 to ≥6/60 (LogMAR <0.48 to ≥1.00) at 25.5%. Meanwhile, in BRVO cases, the highest proportion of visual acuity falls within the group of <6/18 to ≥6/60 (LogMAR <0.48 to ≥1.00) at 41.2%, followed by visual acuity ≥6/12 (LogMAR ≥0.30) at 26.5%. In terms of macular thickness, CRVO cases have thicker macular layers than BRVO cases. In other words, the degree of macular edema and visual impairment in CRVO is generally more severe than in BRVO. These findings are consistent with a study by Silitonga et al., where the mean corrected visual acuity in CRVO was 1.41 ± 0.55 and in BRVO was 0.93 ± 0.48.[24] Another study by Unsal et al. also found that the mean best-corrected visual acuity in retinal vein occlusion was 1.01±0.49, with mean macular thickness of 503.6±118 µm in CRVO and less than 500 µm in BRVO.[25] Additionally, a study by Lee et al. in South Korea found that the mean visual acuity in BRVO was logMAR 0.4 and the central macular thickness was around 500 µm.[26]

The decline in vision in retinal vein occlusion occurs through various combinations of three different mechanisms.[27] First, distal serous exudation to the point of obstruction can cause macular edema. As damage to vascular architecture becomes more severe, this edema can become permanent or prolonged with accompanying degenerative changes (macular holes, epiretinal membranes, etc.). Second, retinal hemorrhage can occur in the area drained by the retinal vein distal to the obstruction; in severe cases, subretinal blood dissection can lead to atrophy and/or retinal pigment epithelium (RPE) scar tissue, often subfoveally. Finally, venous obstruction can be accompanied by ischemic damage to the retina, resulting in the loss of extensive capillary layers and post-ischemic atrophy changes. Significant retinal ischemia can lead to pathological retinal neovascularization, resulting in vitreous hemorrhage and/or tractional retinal detachment; furthermore, iris neovascularization can lead to neovascular glaucoma. Patients with macular edema due to CRVO usually present with mild vision impairment that can even improve over time without intervention.[27] Compared to BRVO, patients with macular edema related to CRVO often experience more significant visual deterioration, which typically worsens over time regardless of intervention. This is related to the differences in occlusion location and pathogenesis between CRVO and BRVO. However, the visual prognosis of patients depends on the retinal perfusion status at the time of occlusion. Patients with "non-ischemic" (or "perfusion") type CRVO often have a relatively benign disease, with macular edema resolving in about 30% of eyes over time (and pathological neovascularization rarely occurs). Meanwhile, in patients with "ischemic" (or "non-perfusion") type CRVO, the likelihood of visual improvement is lower, and the risk of pathological

neovascularization is higher (neovascular glaucoma occurs in about 25% of these cases).

Management of OVR with Macular Edema

In terms of management, there are various combinations of interventions for CRVO and BRVO cases. However, the highest proportion of intervention types is intravitreal anti-VEGF injections, accounting for up to 62.5% of the management of CRVO and BRVO cases. The next most commonly performed intervention is photocoagulation laser therapy, which in this study was combined with anti-VEGF injections. In addition, steroid injections and vitrectomy interventions are also performed, albeit with smaller proportions, and they are more often used in combination with anti-VEGF injections. Combination therapy is generally administered when anti-VEGF injection therapy alone is not successful. Based on these findings, it can be said that anti-VEGF therapy is the primary intervention in the study's dataset.

This is consistent with current guidelines, where first-line therapy for macular edema due to CRVO or BRVO is intravitreal anti-VEGF injections.[15] Both ranibizumab (BRAVO and CRUISE studies) and aflibercept (GALILEO/COPERNICUS; VIBRANT studies) have been shown to be effective in treating macular edema. Significant improvements in visual acuity have been demonstrated alongside improvements in macular edema with these therapies. Both types of anti-VEGF drugs are administered every month for the first 6 months of treatment and then as needed according to the respective studies. Bevacizumab is also used off-label to treat macular edema and neovascularization in CRVO and BRVO. In this study, bevacizumab, an anti-VEGF drug, was used. According to the LEAVO study, bevacizumab is more cost-effective than ranibizumab and aflibercept. Although the study could not demonstrate that bevacizumab is inferior to the other two anti-VEGF drugs, their health-related quality of life effects are equivalent.[28] The CVOS study supports panretinal photocoagulation for iris neovascularization. However, the study does not support grid photocoagulation for macular edema. The BVOS study supports the use of grid laser photocoagulation for macular edema. Additionally, the BVOS study group recommends sectoral panretinal photocoagulation for the treatment of retinal neovascularization.[15]

Intravitreal corticosteroid treatment has previously been proven effective for treating macular edema in CRVO.[29] However, this injection comes with significant side effects such as cataract formation and increased intraocular pressure. The SCORE-BRVO study was the largest study that evaluated the safety and efficacy of intravitreal triamcinolone compared to grid laser treatment for macular edema. At the 12-month mark, the study found no difference in visual acuity between the two triamcinolone groups and the laser group. However, there was significant cataract formation and increased intraocular pressure in the intravitreal triamcinolone group. Furthermore, monitoring over three years showed a significant improvement in visual acuity in the laser group compared to the triamcinolone group. Based on these study results, triamcinolone is not recommended as a first-line therapy for macular edema due to CRVO, but rather as an adjuvant therapy to anti-VEGF injections or laser treatment, or as a second-line agent. In cases where complications like neovascularization occur, such as non-clearing vitreous hemorrhage, pars plana vitrectomy may be considered, often combined with intraoperative endolaser to non-perfused retinal areas. Some retinal surgeons also consider pars plana vitrectomy with ILM (internal limiting membrane) peeling for the treatment of refractory macular edema in CRVO, although there are no specific guidelines yet.[29]

Changes in Central Macular Thickness and Visual Acuity After Intervention

Overall, the study findings suggest a reduction in macular thickness and an improvement in visual acuity after intervention, both in CRVO and BRVO cases. Additionally, it was observed that CRVO cases had greater changes in macular thickness before and after intervention than BRVO cases. In cases where both anti-VEGF injection and photocoagulation laser therapy were combined, the reduction in macular edema was greater than with anti-VEGF injections alone.

These results are consistent with a 3-year retrospective cohort study by Costa et al., which found changes in central macular thickness from 538 to 290 μm and changes in visual acuity from 0.7 to 0.4 logMAR in 105 cases of OVR. Macular edema resolution occurred in 51% of patients (56.3% in BRVO cases and 42.5% in CRVO cases). In this study, most patients received anti-VEGF injections with a total median of 10 injections (median of 6 injections in the first year).[30] Similar findings were reported in a study by Vaz-Pereira et al., which showed an improvement in visual acuity from 0.8 to 0.7 logMAR after anti-VEGF injections.[31] A study by Silitonga et al.[24] showed a corrected visual acuity improvement from 1.41 ± 0.55 logMAR to 0.74 ± 0.37 logMAR after injections, with central macular thickness decreasing from 472.1 ± 119.5 μm to 383.8 ± 146.7 μm at month 1 and further to 307.0 ± 98.2 μm at 6 months.

A case study by Dr. Andi Arus Victor showed that a minimum of 2 loading doses of anti-VEGF and monthly monitoring were required for improvement in vision and anatomical structure in non-ischemic CRVO cases.[32] More research is needed on the number of injections and visual outcomes in OVR with macular edema.

Study Limitations

There are several limitations to this descriptive retrospective study. First, there was no standardization of the best-corrected visual acuity examination time or macular thickness assessment time for OVR patients, making it difficult to assess trends in parameter assessment within the same time period. Second, the study did not limit the follow-up time, leading to variations in follow-up time among patients. Additionally, the study sample was collected during a pandemic, resulting in inconsistent timing of monthly loading dose injections and a high rate of lost-to-follow-up cases over time, which led to a significant amount of incomplete data and subsequent exclusions from the study

CONCLUSION

Patients affected by macular edema resulting from retinal vein occlusion (OVR) exhibit distinct demographic and clinical characteristics. Typically, these individuals are aged over 50, predominantly male, and tend to experience OVR in a single eye. Hypertension and diabetes mellitus stand out as the prevailing systemic risk factors associated with this condition. Moreover, a noticeable disparity emerges between central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) cases, with CRVO cases presenting more severe initial visual acuity impairments and thicker macular regions. Anti-VEGF injections serve as the primary therapeutic approach, administered either alone or in combination with other treatments. On average, patients undergo approximately two anti-VEGF injections within the first year, resulting in a reduction in central macular thickness. However, the study suggests that the improvement in visual acuity outcomes remains somewhat limited in both CRVO and BRVO patients.

To enhance the overall care and management of individuals dealing with macular edema due to retinal vein occlusion (OVR), several key strategies should be implemented. Firstly, prioritizing patient education is essential to promote consistent treatment adherence and optimize the scheduling of vital interventions such as anti-VEGF injections. A comprehensive approach to patient care is also crucial, involving the identification and management of systemic risk factors and comorbid conditions. Collaboration with various medical units can facilitate this process, ensuring a well-rounded and integrated approach. Furthermore, efforts to increase public awareness about the systemic risk factors associated with OVR not only contribute to prevention but also foster a broader understanding of the condition among the general populace. Lastly, recognizing the need for further analytical research to explore the intricate relationships between various parameters in macular edema due to OVR is pivotal for refining diagnostic and treatment strategies and ultimately improving patient outcomes.

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