Prognostic Factors for Visual Outcomes in Retinal Vein Occlusion: Real-World Data on Anti-VEGF and Dexamethasone Therapies

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ABSTRACT

Objectives: To evaluate demographic, clinical, and treatment-related factors influencing 12-month visual outcomes in patients with retinal vein occlusion (RVO) treated with intravitreal therapies.

Methods: This retrospective study included 89 treatment-naïve patients with branch RVO (BRVO) or central RVO (CRVO) followed for 12 months at a tertiary center. Patients received intravitreal bevacizumab, aflibercept, dexamethasone implant, or combination therapies. Baseline and follow-up best-corrected visual acuity (BCVA, logMAR) and central macular thickness (CMT) were recorded. Optical coherence tomography (OCT) parameters including serous macular detachment (SMD), hyperreflective foci (HRF), disorganization of the retinal inner layers (DRIL), and external limiting membrane (ELM) integrity were also assessed. Predictors of 12-month logMAR were analyzed using univariate and multivariate linear regression.

Results: The cohort included 65 BRVO (73.0%) and 24 CRVO (27.0%) patients (mean age 63.7 ± 12.1 years; 51.7% male). In univariate analysis, older age (p=0.002), CRVO type (p=0.004), baseline logMAR (p<0.001), baseline CMT (p=0.001), number of injections (p=0.01), HRF (p=0.023), DRIL (p=0.003), and ELM disruption (p=0.01) were significantly associated with poorer 12-month visual outcomes. Combination therapy with bevacizumab+dexamethasone was also linked to worse prognosis (p=0.009). In multivariate analysis (R^2=0.467), only older age (p=0.003) and worse baseline BCVA (p=0.006) remained independent predictors, while baseline CMT, OCT biomarkers, treatment regimen, and occlusion type lost significance.

Conclusions: Age and baseline BCVA are the strongest independent predictors of long-term visual outcomes in RVO. Structural OCT features and treatment types show associations in univariate analyses but are not independent determinants after adjustment, underscoring the predominance of functional baseline status for prognosis.

Keywords: Retinal vein occlusion, anti-VEGF therapy, macular edema, visual acuity

INTRODUCTION

Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy, affecting millions worldwide (1). RVO is classified into two main types: central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), depending on the location of the venous blockage. This condition often leads to visual impairment through complications such as macular edema, retinal ischemia, and neovascularization (1). The resulting impact on quality of life and the associated economic burden highlight the importance of effective management strategies for RVO.

The advent of anti-vascular endothelial growth factor (anti-VEGF) agents has revolutionized the treatment of mac-

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ular edema secondary to RVO. These agents, including Bevacizumab, Aflibercept, and Ranibizumab, target the pathological vascular permeability and neovascularization seen in RVO, offering significant improvements in visual acuity for many patients (2). Additionally, corticosteroid implants such as Dexamethasone have been employed as an alternative or adjunct therapy, particularly in cases with suboptimal response to anti-VEGF monotherapy (3). Despite these advancements, the variability in treatment response necessitates a deeper understanding of the factors influencing therapeutic outcomes.

Although randomized trials and meta-analyses have established the efficacy of anti-vascular endothelial growth factor (anti-VEGF) agents and intravitreal corticosteroids for RVO-related macular edema, prognostic determinants that translate into real-world outcomes remain incompletely defined. The specific gap this study addresses is the lack of real-world evidence that simultaneously examines (i) baseline visual acuity and central macular thickness together with demographic and disease-type factors (BRVO vs CRVO), and (ii) the comparative influence of commonly used treatment approaches—including anti-VEGF monotherapy, dexamethasone implant, and sequential "switch" strategies—on 12-month visual outcomes. By analyzing a heterogeneous, practice-based cohort with multivariable modeling, we aim to provide pragmatic prognostic insights that can inform individualized treatment planning beyond the constraints of clinical trial settings.

Baseline characteristics such as initial visual acuity, the presence of macular edema, and central foveal thickness have been identified as potential predictors of treatment response in RVO patients (4,5). Identifying these factors early can aid in tailoring personalized treatment plans and setting realistic expectations for patients.

This retrospective study aimed to evaluate the demographic, clinical, and treatment-related factors that influence visual outcomes in patients with RVO treated with anti-VEGF agents. By analyzing real-world data from a single tertiary care center, this study seeks to provide valuable insights into the prognostic factors associated with visual improvement and to contribute to the optimization of RVO management strategies.

METHODS

A retrospective evaluation was conducted on patients who were diagnosed with RVO. This study is a retrospective analysis of medical records conducted at the Kocaeli City Hospital. It is a single-center study. The study protocol received approval from the Kocaeli City Hospital ethics committee. The data collected for analysis were anonymised prior to examination. The procedures employed adhered to the standards outlined in the Declaration of Helsinki.

Study Population

We included treatment-naïve patients with branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO), aged ≥20 years, who presented within 12 months of symptom onset and were followed for at least 12 months. If both eyes were affected, only the eye with earlier onset was analyzed.

Exclusion criteria were ischemic RVO, severe cataract (≥Grade 3), glaucoma, diabetic retinopathy beyond mild nonproliferative stage, ocular ischemic syndrome, uveitis or vasculitis, arterial occlusion, or prior intraocular treatments for RVO (injection, laser, vitrectomy). Patients with a history of major ocular surgery other than uncomplicated cataract extraction were also excluded.

Baseline demographic and systemic data, including age, sex, laterality, hypertension, and diabetes mellitus, were obtained from medical records. Although fluorescein angiography (FA) was routinely performed at baseline, macular ischemia status was not consistently documented. Other potential systemic risk factors (dyslipidemia, cardiovascular disease, smoking) could not be reliably assessed due to incomplete documentation.

Ocular Examinations

The fundus examination was conducted to determine the kind of RVO (central or branch), the existence of any abnormalities in the optic disc, macular edema, neovascularization in the disc or elsewhere, the extent of retinal hemorrhage, and other abnormal findings such as vitreous hemorrhage. This study classified eyes with hemiretinal vein occlusion as eyes with CRVO and included them in the CRVO group. FA was routinely performed at baseline, but ischemia status was not consistently documented. *Best Corrected Visual Acuity and Central Macular Thickness*

Baseline and 12th month best corrected visual acuity (BCVA) and central macular thickness (CMT) were scanned. At the initial examination, the existence of serous macular detachment (SMD) was also documented. In addition to CMT and the presence of SMD, OCT parameters including hyperreflective foci (HRF), disorganization of the retinal inner layers (DRIL), and the integrity of the external limiting membrane (ELM) were evaluated.The BCVA was assessed using a conventional Snellen decimal visual acuity chart positioned at a distance of 5 meters. The visual acuities for "counting fingers" and "hand movement" were translated to decimal values of 0.014 and 0.004, respectively (3). Decimal values were transformed into logarithmic form using the least angle of resolution (logMAR) for statistical analysis.

Treatment

Patients were divided into treatment groups according to 1.intravitreal anti VEGF injection group (Bevacizumab, Aflibercept, intravitreal Bevacizumab + Aflibercept injection) 2. Dexamethasone implant group, 3. intravitreal Dexamethasone implant + Bevacizumab injection groupAll patients were treated according to a pro re nata (PRN) protocol. After the diagnosis of RVO-related macular edema, an intravitreal anti-VEGF injection (bevacizumab, ranibizumab, or aflibercept) was administered within the first two weeks. During the initial 12 months, patients were examined monthly, and repeat injections were performed if macular edema persisted on OCT. In selected pseudophakic patients with normal intraocular pressure who declined monthly follow-up visits, a dexamethasone intravitreal implant was considered as an alternative treatment option.

Statistical Analysis

Statistical analyses were performed to evaluate the predictors of 12-month visual outcomes (12.M LogMAR) in patients with retinal vein occlusion. Descriptive statistics, including means, medians, standard deviations, and percentages, were used to summarize baseline demographic and clinical characteristics. Univariate linear regression analysis was conducted to explore the relationship between potential predictors—such as age, sex, diagnosis type (CRVO vs. BRVO), baseline visual acuity (0.M LogMAR), baseline CMT (0.M CMT), SMD, and the number of injections and 12-month LogMAR visual acuity. Additionally, treatment types were analyzed as predictors in a separate univariate regression model. Multivariate linear regression analysis was performed to identify independent predictors of 12-month LogMAR while adjusting for confounding variables. Statistical significance was set at p <0.05, and the coefficient of determination (R^2) was reported to quantify the proportion of variance explained by each model. All analyses were conducted using Jamovi (Version 2.5) program.

RESULTS

A total of 89 patients were included in the study, with a mean age of 63.75 ± 12.09 years. The study consisted of 46 males (51.7%) and 43 females (48.3%). Among the diagnoses, 65 patients (73.0%) had branch retinal vein occlusion (BRVO), and 24 patients (27.0%) had central retinal vein occlusion (CRVO). Hypertension was present in 56 patients (63,9 %) and absent in 33 patients (37,1%). Diabetes mellitus was present in 28 patients (31.5 %) and absent in 61 patients (68.5 %).

Table 1. *Demographic and Clinical Characteristics of Study Participants at Baseline and 12-Month Follow-up*

Variables	N	Mean	Median	SD
Age	89	63.753	66	12.091
0.M LogMAR	89	0.848	0.699	0.525
0.M CMT	89	552.798	506	234.024
12.M LogMAR	89	0.786	0.523	0.641
12.M CMT	89	340.697	278	171.201

M: Month, CMT: Central macular thickness, SD: Standart deviation

Table 2. *Baseline Distribution of Demographic and Clinical Characteristics of Study Participants*

Variables		Counts	% of Total
Sex	M	46	51.7%
	F	43	48.3%
Dx	BRVO	65	73.0%
	CRVO	24	27.0%
Treatment	Bevacizumab	56	62.9%
	Aflibercept	7	7.9%
	Dexamethasone	6	6.7%
	Bevacizumab+Aflibercept	3	3.4%
	Bevacizumab+Dexamethasone	17	19.1%
SMD	Absent	48	53.9%
	Present	41	46.1%
HT	Absent	33	37.1 %
	Present	56	62.9 %
DM	Absent	61	68.5 %
	Present	28	31.5 %

M: Male, F: Female, Dx: Diagnosis, BRVO: Branch retinal vein occlusion, CRVO: Central retinal vein occlusion, SMD: Serous macular detachment, HT: Hypertension, DM: Diabetes mellitus

Serous macular detachment was observed in 46.1% of eyes. Regarding treatment distribution, 62.9% of patients received bevacizumab monotherapy, while 7.9% received aflibercept, 6.7% dexamethasone implant, 3.4% a combination of bevacizumab and aflibercept, and 19.1% a combination of bevacizumab and dexamethasone.

At baseline, the mean best-corrected visual acuity (BCVA) was 0.848 ± 0.525 LogMAR and the mean central macular thickness (CMT) was 552.8 ± 234.0 µm. At the 12-month follow-up, mean BCVA improved to 0.786 ± 0.641 LogMAR, while mean CMT decreased to 340.7 ± 171.2 µm.

Univariate Analyses

In univariate linear regression analysis, several demographic and clinical parameters were significantly associated with 12-month logMAR visual acuity. Older age ($\beta = 0.0169$, $p = 0.002$, $R^2 = 0.102$) and the presence of central retinal vein occlusion (CRVO) ($\beta = 0.43$, $p = 0.004$, $R^2 = 0.09$) were predictors of poorer visual outcomes. Baseline logMAR visual acuity ($\beta = 0.64$, $p < 0.001$, $R^2 = 0.28$) and baseline central macular thickness (CMT) ($\beta = 0.34$, $p = 0.001$, $R^2 = 0.11$) also emerged as significant determinants of 12-month visual acuity.

Additionally, the number of injections ($\beta = 0.34$, $p = 0.01$, $R^2 = 0.12$), the presence of fine hyperreflective foci (HRF) ($\beta = 0.52$, $p = 0.023$, $R^2 = 0.07$), disorganization of retinal inner layers (DRIL) ($\beta = 0.418$, $p = 0.003$, $R^2 = 0.1$), and disrupted external limiting membrane (ELM) integrity ($\beta = –0.35$, $p = 0.01$, $R^2 = 0.07$) were significantly associated with worse visual acuity. In contrast, sex, hypertension, diabetes mellitus, and the presence of serous macular detachment (SMD) were not significantly related to 12-month visual outcomes (Table 3)

Table 3. *Univariate Linear Regression Analysis of Factors Associated with 12-Month LogMAR Visual Acuity*

Predictor	Beta	P	R^2
Age	0.0169	0.002	0.102
Sex	-0.04	0.76	0.001
CRVO - BRVO	0.43	0.004	0.09
0. Month LogMAR	0.64	<0.001	0.28
0. Month CMT	0.34	0.001	0.11
SMD	0.13	0.35	0.01
Number of Injections	0.34	0.01	0.12
HT	-0.07	0.61	0.003
DM	-0.09	0.54	0.004
HRF: Fine – None	0.52	0.023	0.07
HRF: Confluent – None	-0.10	0.81	070.
DRIL	0.418	0.003	0.1
ELM	-0.35	0.01	0.07

CRVO: Central retinal vein occlusion, BRVO: Branch retinal vein occlusion, CMT: Central macular thickness, SMD: Serous macular detachment, HT: Hypertension, DM: Diabetes mellitus

Treatment-Specific Analyses

When treatment types were compared using univariate regression, antiVEGF group served as the reference. Patients receiving the combination of bevacizumab and dexamethasone demonstrated significantly worse 12-month visual acuity compared to the antiVEGF group ($\beta = 0.45$, $p = 0.009$, $R^2 = 0.08$). No significant difference was observed between the dexamethasone implant group and the antiVEGF group ($p = 0.76$). (Table 4)

Multivariate Analyses

In multivariate linear regression analysis ($R^2 = 0.467$), only age ($\beta = 0.283$, $p = 0.003$) and baseline logMAR visual acuity ($\beta = 0.303$, $p = 0.006$) remained independently associated with 12-month visual outcomes. Baseline CMT ($p = 0.061$), number of injections ($p = 0.914$), type of occlusion (CRVO vs. BRVO, $p = 0.354$), treatment regimen ($p > 0.65$), HRF ($p > 0.3$), DRIL ($p = 0.367$), and ELM status ($p = 0.112$) did not reach statistical significance in the multivariate mode. (Table 5)

Table 4. *Univariate Linear Regression Analysis of 12-Month LogMAR Visual Acuity Based on Treatment Types*

Treatment (Ref: Bevacizumab)	Beta	p	R^2
Dexamethasone – Bevacizumab	–0.08	0.76	0.08
Bev + Dexa – Bevacizumab	0.45	0.009	0.08

Table 5. *Multivariate Linear Regression Analysis of Predictors for 12-Month LogMAR Visual Acuity*

Predictor	β (Stand.)	Estimate	p	R^2
Age	0.283	0.0156	0.003	
Baseline LogMAR (0M)	0.303	0.3759	0.006	
Baseline CMT (0M SFT)	0.201	0.00057	0.061	
Number of Injections	0.014	0.0140	0.914	
CRVO vs BRVO	0.196	0.1279	0.354	
Dexamethasone – Bevacizumab	0.165	0.1076	0.694	
Bev + Dexamethasone – Bevacizumab	0.139	0.0908	0.659	
HRF: Fine – None	0.186	0.1215	0.342	
HRF: Confluent – None	–0.052	–0.0339	0.889	
DRIL: present – absent	0.180	0.1176	0.367	
ELM: disrupted – intact	–0.307	–0.2005	0.112	0.467

DISCUSSION

In this retrospective analysis of patients with retinal vein occlusion (RVO) treated with intravitreal therapies, we identified several demographic, clinical, and anatomical factors influencing visual outcomes at 12 months. The main findings can be summarized as follows: (i) older age and worse baseline visual acuity were independently associated with poorer visual prognosis; (ii) baseline central macular thickness (CMT), number of injections, presence of fine hyperreflective foci (HRF), disorganization of the retinal inner layers (DRIL), and external limiting membrane (ELM) disruption were correlated with visual outcomes in univariate analysis, but lost significance in the multivariate model; and (iii) patients who received a combination of bevacizumab and dexamethasone had inferior visual outcomes compared to those treated with bevacizumab monotherapy.

Our findings confirm that baseline visual acuity (BCVA) and central macular thickness (CMT) were the strongest predictors of visual outcomes at 12 months. Patients presenting with poorer baseline BCVA experienced greater relative improvement, which is in line with the concept that eyes with more severe functional impairment may retain greater potential for recovery when treated promptly. Conversely, higher baseline CMT was associated with worse outcomes, consistent with the understanding that chronic macular edema causes structural damage and photoreceptor dysfunction that limit long-term recovery potential.

The presence of serous macular detachment (SMD) did not show a significant association with visual prognosis in our cohort. While Firat et al. (16) demonstrated that visual gains were less sustainable in patients with SMD compared to those without, our results suggest that SMD alone may not be as decisive as BCVA or CMT in predicting outcomes. This discrepancy may reflect differences in sample size, follow-up duration, or patient selection criteria, and highlights the need for larger prospective studies to further clarify the role of SMD.

Similarly, the number of intravitreal injections was not significantly associated with visual outcomes after adjustment for baseline parameters. This likely reflects variability in individual treatment needs and disease course rather than ineffectiveness of repeated injections. In clinical practice, these findings underscore that treatment frequency should be individualized, and that visual prognosis depends more on initial functional and anatomical status than on the absolute number of injections received.

Although we incorporated additional OCT biomarkers such as HRF, DRIL, and the integrity of ELM and EZ into

our analysis, their effects on long-term visual outcomes were not statistically significant in our study population. This may be explained by the relatively small sample size and retrospective design, which could have limited statistical power. Previous reports have suggested that these OCT features are important prognostic markers, and our findings highlight the need for larger prospective studies to better clarify their role in retinal vein occlusion.

Age has been shown as a risk factor for retinal vein occlusion and serves as a predictive factor for the responsiveness to bevacizumab therapy in patients with central retinal vein occlusion (CRVO). (8,9) Age was identified as an independent predictor of 12-month visual acuity, with older patients exhibiting poorer outcomes alignts with the previous studies.(10-12) This finding may reflect age-related factors, such as reduced retinal resilience and underlying comorbidities, which could limit the response to treatment. Also it was assumed that age-related sclerotic changes in arteries and degenerative changes in vascular walls may be related to this finding.

The significant association between CRVO and worse visual outcomes compared to BRVO is consistent with the understanding that CRVO often involves more extensive retinal ischemia and damage. (13,14)

While univariate analysis suggested a significant effect of the combination of bevacizumab and dexamethasone compared to bevacizumab monotherapy, this was not sustained in the multivariate model. The lack of statistical significance for treatment types in the multivariate analysis suggests that the therapeutic response in RVO is primarily influenced by baseline disease characteristics rather than the specific anti-VEGF agent or corticosteroid used. These findings align with previous reports indicating comparable efficacy among different anti-VEGF agents in the treatment of RVO-associated macular edema. (15) Of note, treatment groups were heterogeneous, including different anti-VEGF agents and the dexamethasone implant. Because of the small number of patients in some subgroups, the statistical power was limited. Therefore, our findings mainly reflect the influence of baseline disease characteristics rather than the specific treatment type. This heterogeneity was acknowledged as a limitation of the study. However, the observed improvement in visual outcomes with combination therapy warrants further investigation in larger cohorts to determine whether certain patient subgroups benefit more from such strategies.

Regarding treatment type, although univariate analysis suggested some differences, these associations did not remain significant after adjustment for baseline factors. This indicates that real-world outcomes are largely driven by disease characteristics at presentation rather than the specific anti-VEGF agent used. Clinically, this underscores that treatment selection should be guided less by expectations of efficacy differences among agents and more by considerations such as safety profile, injection burden, cost, and patient comorbidities (Sangroongruangsri et al., 2018; Light et al., 2021). From a patient counseling perspective, these results reinforce the need to set realistic expectations: while anti-VEGF therapy is highly effective overall, visual recovery potential depends primarily on baseline BCVA and macular thickness rather than the choice of a particular agent.

This study's retrospective design and reliance on real-world data from a single tertiary care center contribute to its strength by reflecting clinical practice. However, several limitations should be acknowledged. The relatively small sample size and lack of randomization may limit the generalizability of the findings. Since the study was retrospective in nature, we had very little data regarding when the symptoms first appeared. This is another limitation of our study. Another limitation of this study is the absence of certain systemic and ocular risk factors in the retrospective medical records, including the duration of macular edema, presence of dyslipidemia, smoking status, and obesity. Since these variables were not systematically documented, they could not be incorporated into the analysis. Their absence may have influenced treatment response and visual prognosis. Heterogeneity of treatment types (different anti-VEGF agents and corticosteroid implant) may have influenced treatment responses. Due to the small subgroup sizes, separate analyses were underpowered, and this should be interpreted with caution. Although fluorescein angiography (FA) was performed in all patients at the initial visit, the presence or absence of macular ischemia was not systematically documented in the patient records. Future studies with larger, prospective cohorts and more comprehensive data collection are needed to validate these findings and further explore the role of treatment combinations.

In conclusion, this study highlights the pivotal role of baseline visual acuity and macular thickness in predicting visual outcomes in RVO patients treated with anti-VEGF agents. Age and the type of RVO also influence long-term prognosis. These findings underscore the importance of early and individualized treatment strategies tailored to baseline disease characteristics to optimize visual outcomes in RVO patients.

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