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ORIGINAL RESEARCH

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Factors influencing ranibizumab efficacy and prognosis of patients with retinal vein occlusion and macular edema based on systemic inflammatory indexes and OCT parameters

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Abstract

This study aimed to investigate the effects of ranibizumab on optical coherence tomography (OCT) parameters and the peripheral blood systemic inflammation index in men diagnosed with retinal vein occlusion accompanied by macular edema (BRVO-ME) and explore the relevant factors affecting visual prognosis. The clinical data of men diagnosed with BRVO-ME who underwent vitreous cavity injections of ranibizumab were retrospectively analyzed, and they were stratified into a good prognosis group (defined as a difference ≤ -0.3) and a poor prognosis group (defined as a difference > -0.3) based on the difference between the logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) and pre-treatment logMAR BCVA at 6 months post-treatment. After 6 months of ranibizumab treatment, there were significant reductions ($p < 0.05$) observed in logMAR BCVA, intraocular pressure, center macular thickness (CMT), outer hyperreflective retinal foci (HRFs), inner HRFs, outer membrane (ELM) integrity, elliptical zone (EZ) integrity, as well as serum neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and systemic immune-inflammatory index (SII) levels. Disease duration, ELM integrity, BCVA, outer HRF and serum SII emerged as independent risk factors influencing the prognosis of visual acuity subsequent to ranibizumab treatment in BRVO-ME eyes ($p < 0.05$). A nomogram prediction model incorporating these risk factors exhibited favorable differentiation and accuracy. In conclusion, disease duration, BCVA, ELM integrity, presence of outer HRF and elevated serum SII were identified as independent risk factors influencing visual prognosis following ranibizumab treatment in male patients with BRVO-ME. Furthermore, the nomogram developed based on OCT parameters and serum SII exhibited favorable differentiation and accuracy.

Keywords

Retinal vein occlusion; Ranibizumab; Macular edema; Optical coherence tomography; Inflammation

1. Introduction

Retinal vein occlusion (RVO) is a prevalent retinal vascular ailment in males, ranking second only to diabetic retinopathy. Epidemiological studies suggest RVO prevalence ranging from 0.3% to 2.1%, with rates among individuals over 40 years old ranging from 1% to 2% [1]. Vascular blockage can be divided into two categories: branch retinal vein obstruction (BRVO) and central retinal vein obstruction (CRVO), depending on the location of the obstruction. Due to common habits such as smoking and alcohol consumption, men often experience various complications, including macular edema (ME), which represents a frequent clinical manifestation of RVO and a significant cause of vision impairment, visual distortion and potential blindness. Additionally, research has indicated that ME could be correlated with smoking habits [2].

Studies have demonstrated that elevated levels of retinal vascular endothelial growth factor (VEGF) are the primary cause of ME secondary to branch retinal vein occlusion (BRVO-ME). In recent years, anti-VEGF drug therapy has proven effective in reducing ME and improving visual acuity, becoming the primary treatment for BRVO. In addition, it has been shown that intravitreal injection of ranibizumab, a Fab antibody fragment neutralizing all isoforms of VEGF-A, could improve diabetic ME (DME) [3]. However, there are significant differences in visual acuity recovery among patients treated with anti-VEGF medication, with some experiencing unsatisfactory outcomes despite symptom relief. Therefore, investigating the factors influencing visual prognosis after anti-VEGF drug treatment

in BRVO-ME is crucial for enhancing clinical efficacy and improving patients' visual acuity.

Currently, optical coherence tomography (OCT) has become a valuable tool for the early diagnosis of RVO and for monitoring the morphological changes in the retinal macula before and after treatment. Specific imaging features identified by OCT have become biomarkers for assessing the prognosis of RVO. The systemic immune-inflammatory index (SII), platelet/lymphocyte ratio (PLR), and peripheral blood neutrophil/lymphocyte ratio (NLR) are three novel systemic inflammatory indices associated with cardiovascular disease and cancer. NLR, PLR and SII are considered standard diagnostic parameters for various conditions due to their cost-effectiveness and simple calculation process [4]. Elevated levels of PLR, NLR and SII could be considered potential markers of RVO [5]. However, the relationship between PLR and NLR and the visual prognosis following ranibizumab treatment in eyes affected by BRVO-ME remains unknown.

In this present study, we evaluated ranibizumab's efficacy in male BRVO-ME patients based on OCT parameters and the levels of PLR, NLR and SII. We also explored factors influencing visual prognosis, based on which a nomogram was developed to predict poor outcomes post-ranibizumab treatment.

2. Materials and methods

2.1 Patients

A retrospective analysis was conducted on the clinical data from men diagnosed with BRVO-ME who received vitreous cavity injections of ranibizumab between January 2019 and January 2022 at The First People's Hospital of Zunyi (the Third Affiliated Hospital of Zunyi Medical University).

The study inclusion criteria were as follows: (1) age $\geq$18 years; (2) male; (3) presenting with symptoms such as blurred vision, decreased visual acuity, and/or visual distortion, and diagnosed with BRVO-ME through slit microscope anterior view, fundus photography, fundus angiography fluorescence angiography (FFA) and OCT; (4) onset occurring in one eye only; (5) first-time onset; (6) no prior relevant treatment; (7) treated with vitreoretinal ranibizumab following a 1 + PRN regimen; (8) surgical tolerance without contraindications; and (9) completion of regular follow-up after treatment.

Moreover, the exclusion criteria were: (1) concurrent diagnosis of glaucoma and other fundus conditions such as diabetic retinopathy, age-related macular degeneration, high myopic fundus disease, choroidal neovascularization, and optic neuropathy; (2) BRVO with complications like iris neovascularization, vitreous hemorrhage, or severe comorbidities affecting visual function; (3) history of prior ocular surgeries; (4) recent use of anticoagulant or antiplatelet medications; (5) presence of active systemic inflammatory disease or hemodynamic disorders within the last three months; and (6) concurrent diagnosis of malignancy.

A total of 130 male patients (130 eyes) meeting the criteria were ultimately included in the study (Fig. 1). This retrospective study was conducted following the principles outlined in the Declaration of Helsinki [6].

2.2 Data collection

(1) General data: Clinical information was retrieved from patients' electronic medical records, encompassing age, body mass index (BMI), disease duration, BRVO-ME characteristics, ME subtype, smoking and alcohol habits, presence of hypertension, diabetes mellitus, heart disease, and hyperlipidemia. (2) Ophthalmologic examination data: Best-corrected visual acuity (BCVA) was assessed using the international standard visual acuity chart, with results converted to a logarithmic minimum angle of resolution (logMAR) for statistical analysis. Spectralis domain OCT (SD-OCT, Heidelberg Engineering, Heidelberg, Germany) was used to measure center macular thickness (CMT) and to identify the number of hyperreflective retinal foci (HRF) in both inner and outer retinal layers. Additionally, the integrity of the outer limiting membrane (ELM) and ellipsoid zone (EZ) was assessed. (3) Blood examination data: After hospital admission, fasting elbow venous blood samples of 3–5 mL were collected, and the serum was extracted. Neutrophil counts, lymphocyte counts and platelet counts were determined using a fully automatic hematology analyzer. The NLR was calculated as neutrophil count divided by lymphocyte count, the PLR was calculated as platelet count divided by lymphocyte count, and the SII was calculated as platelet count multiplied by neutrophil count divided by lymphocyte count.

2.3 Treatment methods

Preoperative preparation. Levofloxacin eye drops (H20150279, Shentian Pharmaceutical Co.Ltd, China) were instilled into the conjunctival sac 3 days prior to surgery to prevent infection, with 1–2 drops per application, administered 4 times daily. The conjunctival sac was irrigated and sterilized before surgery, adhering strictly to intraocular surgery standards.

Surgical treatment. Anesthesia was achieved using topical oxybuprocaine hydrochloride eye drops (H20056587, BauschLomb, Shandong, China). The conjunctival sac was disinfected with povidone-iodine (50 g/L) for 90 seconds, followed by saline rinsing. Ranibizumab (10 mg/mL, 0.2 mL per vial; SJ20170003, Novartis Pharma Schweiz AG, Global Development, Basel, Switzerland) was injected into the vitreous cavity using a triptych needle, positioned 3.5–4.0 mm behind the corneal limbus either superiorly temporal or superiorly nasal to the ciliary body flat.

Postoperative management. On the first postoperative day, routine dressing changes were conducted to assess intraocular pressure (IOP) and anterior chamber reaction. Levofloxacin eye drops and tobramycin eye drops (Tobrex, H20091082, Alcon-Couvreur, Fort Worth, Texas, USA) were administered to the operated eye 4 times daily for 1 week postoperatively. Follow-up appointments were scheduled at 1 week, 2 weeks and 1 month after each vitreous cavity injection to monitor visual acuity, IOP and fundus status. The decision for re-injection treatment was made at the 1-month postoperative visit based on visual acuity and fundus condition. In cases where fundus angiofluorography revealed non-perfusion zones in the retina, fundus laser photocoagulation was also performed.

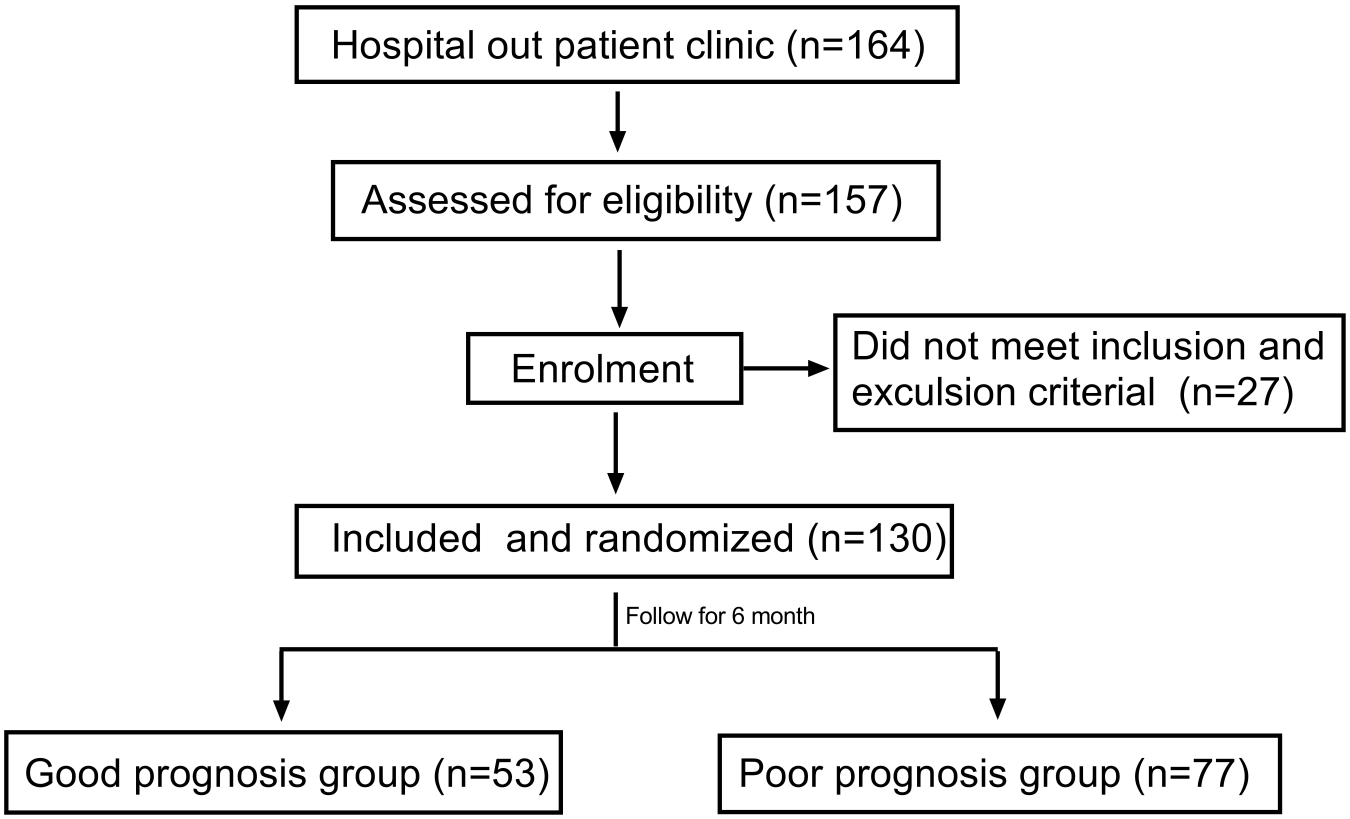

FIGURE 1. Flow diagram illustrating participant enrollment and grouping in the study.

2.4 Follow-up

Follow-up visits were conducted monthly for 6 consecutive months post-treatment, utilizing the same equipment and methods employed for the initial examinations. Based on the difference between logMAR BCVA and pre-treatment logMAR BCVA at the 6-month follow-up, the 130 eyes from 130 male patients were classified into either a good prognosis group (difference ≤ -0.3) or a poor prognosis group (difference > -0.3) (Fig. 1).

2.5 Statistical analysis

Statistical analysis was conducted using the SPSS v24.0 software (IBM Corp., Armonk, NY, USA). Normally distributed measurements are presented as mean $\pm$ standard deviation, and paired *t*-tests were used for pre- and post-treatment visual acuity and CMT values. Continuous variables not conforming to normal distribution are expressed as median (P25, P75) and analyzed using the Kruskal-Wallis test. Multivariate logistic regression analyses were performed to identify risk factors influencing effective improvement in visual acuity at the final follow-up. Logistic regression analyses were based on univariate results, with factors showing statistical significance in the one-factor analysis considered independent variables and prognosis as the dependent variable. Multivariate logistic regression was employed to analyze independent risk factors affecting vision prognosis after ranibizumab treatment. The R (version 4.2.3) software and the rms program package were used to construct a nomogram prediction model based on the identified independent risk factors. Discrimination of the model was assessed using receiver operating characteristic (ROC) analysis. Internal validation of the prediction model was performed through calibration curves and calculation of the consistency index (C-index). A p-value < 0.05 was considered indicative of statistical significance.

3. Results

3.1 Comparison of BCVA and outer retinal morphology before and after treatment

The logMAR BCVA, IOP, CMT, outer HRF and inner HRF were found to be significantly reduced in patients post-treatment compared to pre-treatment ($p < 0.05$, Table 1). In addition, the proportion of missing ELM and EZ were also significantly reduced post-treatment than pre-treatment ($p < 0.05$, Table 1).

3.2 Comparison of peripheral systemic inflammation indexes before and after treatment

Compared with the pre-treatment period, the serum levels of NLR, PLR and SII of the male patients were significantly reduced post-treatment ($p < 0.05$, Table 2).

3.3 Complications

In this study, one patient experienced elevated IOP of 29.3 mmHg (1 mmHg = 0.133 kPa) 1 day post-surgery, requiring treatment with Parisian eye drops twice daily. The IOP returned to the normal range after 3 days. No other patients

TABLE 1. Comparison of outer retinal layer morphology before and after treatment.

Variables	n	Pre-treatment	Post-treatment	t/χ^2	p
logMAR BCVA	130	0.82 ± 0.23	0.56 ± 0.21	9.518	<0.001
Intraocular pressure (mmHg*)	130	15.04 ± 2.71	13.83 ± 3.83	2.940	<0.001
CMT (μm)	130	381.59 ± 70.83	211.72 ± 69.01	19.586	<0.001
HRF number					
Outer layer	130	7.06 ± 0.34	5.37 ± 1.07	17.163	<0.001
Inner Layer	130	56.75 ± 3.37	46.78 ± 11.52	9.471	<0.001
ELM integrity					
Complete		31	72	21.734	<0.001
Missing		99	68		
EZ Integrity					
Intact		27	69	28.238	<0.001
Missing		103	61		

*Note: *1 mmHg = 0.133 kPa. logMAR: logarithm of the minimum angle of resolution; BCVA: best-corrected visual acuity; CMT: center macular thickness; HRF: hyperreflective retinal foci; ELM: outer membrane; EZ: elliptical zone.*

TABLE 2. Comparison of peripheral systemic inflammation indexes before and after treatment.

Variables	n	Pre-treatment	Post-treatment	t	p
NLR	130	4.36 ± 1.25	3.29 ± 1.01	7.591	<0.001
PLR	130	189.35 ± 22.74	156.15 ± 45.19	7.483	<0.001
SII	130	974.62 ± 157.83	787.03 ± 284.25	6.578	<0.001

NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; SII: systemic immune-inflammatory index.

exhibited elevated IOP. Additionally, none of the patients developed ocular complications such as conjunctival hemorrhage, anterior chamber reaction, endophthalmitis, cataract or retinal detachment. Furthermore, no systemic complications related to vitreous injection of anti-VEGF were observed.

3.4 Univariate logistic regression analysis

Based on the difference between logMAR BCVA and pre-treatment logMAR BCVA at 6 months post-treatment, 130 cases comprising 130 eyes were classified into either a good prognosis group (difference ≤ -0.3) or a poor prognosis group (difference > -0.3). Comparative analysis showed no significant differences in BMI, BRVO-ME typology, hypertension, hyperlipidemia, diabetes mellitus, post-treatment localized subconjunctival hemorrhage, number of injections, axial length of the eye, IOP and diurnal variation of IOP between patients in the good prognosis group and those in the poor prognosis group ($p > 0.05$). However, statistically significant differences were observed in age, disease duration, ELM integrity, EZ integrity, BCVA, CMT, outer HRF, inner HRF, PLR, NLR and SII between the two groups ($p < 0.05$, Table 3).

3.5 Multivariate logistic regression analysis

Multivariate logistic regression analysis revealed that disease duration, ELM integrity, BCVA and presence of outer layer HRF were independent risk factors influencing visual acuity prognosis following ranibizumab treatment in men diagnosed with BRVO-ME ($p < 0.05$, Table 4).

3.6 Nomogram model construction and validation

A nomogram prediction model was developed based on disease duration, ELM integrity, BCVA, and presence of outer HRF (Fig. 2A). Individual scores for each risk factor were summed to calculate a total score, which corresponded to the predicted probability of a poor visual acuity prognosis in eyes with BRVO-ME following ranibizumab treatment. The area under the receiver operating characteristic curve (AUC) for the nomogram predicting poor visual acuity prognosis in BRVO-ME eyes treated with ranibizumab was 0.992 (0.983–1.000), indicating excellent discriminatory power (Fig. 2B). Further analysis showed that the concordance index (C-index) of the nomogram model was 0.992 (0.983–1.000), indicating strong consistency. Moreover, calibration curves demonstrated good agreement between predicted and observed probabilities (Fig. 2C), indicating reliable predictive accuracy of the nomogram model in estimating the risk of poor visual prognosis in BRVO-ME eyes treated with ranibizumab, and clinical decision curves illustrated positive net benefit across a threshold probability range of 0.01 to 0.95, indicating effective clinical utility in predicting poor visual acuity prognosis in BRVO-ME eyes treated with ranibizumab (Fig. 2D).

4. Discussion

Ranibizumab, an artificially modified monoclonal antibody belonging to the second generation of recombinant monoclonal antibodies, can effectively bind to VEGF, thereby inhibiting

TABLE 3. Univariate analysis of factors affecting visual prognosis post-ranibizumab treatment in the affected eyes of patients diagnosed with BRVO-ME.

Variables	Good prognosis group (n = 77)	Poor prognosis group (n = 53)	t/χ^2	p
Age (yr)	56.95 ± 5.85	58.56 ± 6.12	1.513	0.133
BMI (kg/m^2)	24.18 ± 1.25	24.24 ± 1.32	0.263	0.793
Smoking				
Yes	29	19	0.044	0.833
No	48	34		
Drinking alcohol				
Yes	30	21	0.006	0.939
No	47	32		
Hypertensive				
Yes	25	17	0.002	0.963
No	52	36		
Hyperlipidemia				
Yes	14	10	3.337	0.068
No	63	43		
Diabetes				
Yes	23	16	0.002	0.969
No	54	37		
Duration of disease (wk)	16.33 ± 2.38	26.60 ± 5.94	13.682	<0.001
BRVO-ME classification				
Ischemic	27	19	0.008	0.927
Non-ischemic type	50	34		
ME type				
Intraretinal fluid type	24	16		
Subretinal fluid type	28	20	0.027	0.986
Mixed type	25	17		
ELM integrity				
Complete	47	15	13.486	<0.001
Missing	30	38		
EZ integrity				
Intact	50	19	10.663	0.001
Missing	27	34		
Number of injections	2.92 ± 0.88	2.95 ± 0.74	0.203	0.839
Length of eye axis (mm)	22.62 ± 0.56	22.51 ± 0.63	1.046	0.298
Intraocular pressure (mmHg*)	13.81 ± 4.14	13.86 ± 3.50	0.072	0.943
Difference between diurnal and nocturnal variation in intraocular pressure (mmHg*)	4.92 ± 1.41	4.97 ± 1.50	0.194	0.847
logMAR BCVA	0.49 ± 0.17	0.71 ± 0.19	7.817	<0.001
CMT (μm)	295.65 ± 67.68	335.07 ± 65.36	3.309	0.001

neovascularization and improving vascular permeability. It is predominantly utilized in the treatment of wet age-related macular degeneration, diabetic retinopathy, high myopia and RVO-induced fundopathy, with notable therapeutic efficacy. Initially approved by the U.S. Food and Drug Administration (FDA) for the treatment of RVO-ME in 2010, ranibizumab was recommended for use by the European Union expert panel for the treatment of RVO in 2011 [7]. Numerous studies have highlighted its remarkable effectiveness in rapidly reducing macular retinal edema and enhancing patients' visual acuity

TABLE 3. Continued.

Variables	Good prognosis group (n = 77)	Poor prognosis group (n = 53)	t/χ^2	p
HRF number				
Outer layer	4.49 ± 0.17	6.63 ± 0.20	66.013	<0.001
Inner Layer	42.05 ± 9.01	53.64 ± 11.50	6.424	<0.001
NLR	3.00 ± 0.91	3.70 ± 1.02	4.135	<0.001
PLR	142.51 ± 34.65	175.97 ± 51.74	4.419	<0.001
SII	677.74 ± 129.46	952.84 ± 263.74	7.885	<0.001

*Note: *1 mmHg = 0.133 kPa. BMI: body mass index; BRVO: branch retinal vein occlusion; ME: macular edema; ELM: outer membrane; EZ: elliptical zone; logMAR: logarithm of the minimum angle of resolution; BCVA: best-corrected visual acuity; CMT: center macular thickness; HRF: hyperreflective retinal foci; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; SII: systemic immune-inflammatory index.*

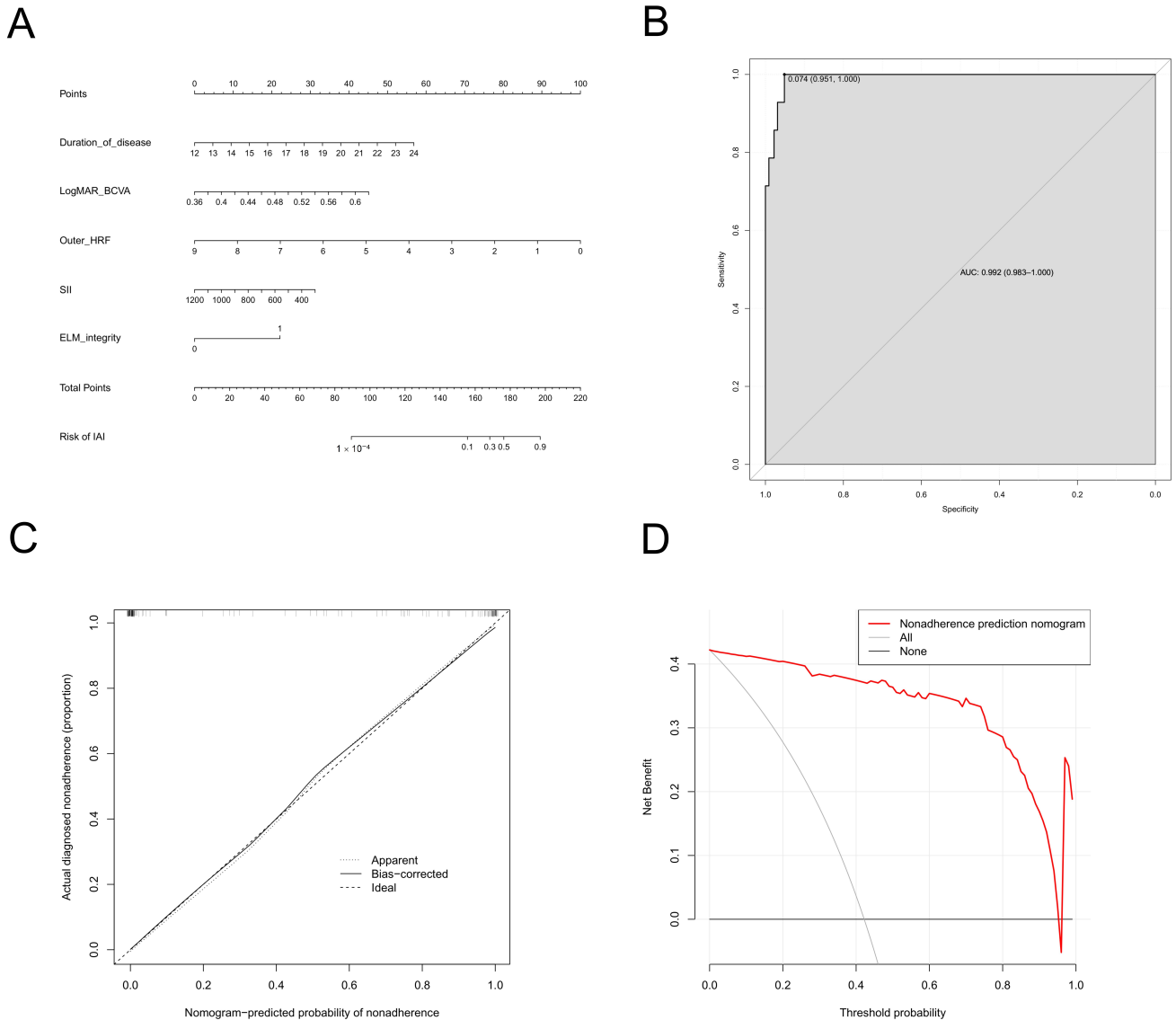

FIGURE 2. Construction and validation of the nomogram. (A) Nomogram model for predicting prognosis in eyes with BRVO-ME treated with ranibizumab. (B) Receiver operating characteristic (ROC) curve assessing the discriminative ability of the nomogram. (C) Calibration curve illustrating the agreement between observed and predicted outcomes of the nomogram. (D) Decision curve analysis evaluating the clinical utility of the nomogram. logMAR: logarithm of the minimum angle of resolution; HRF: hyperreflective retinal foci; SII: systemic immune-inflammatory index.

TABLE 4. Multivariate analysis of factors affecting visual acuity prognosis post-ranibizumab treatment in BRVO-ME eyes.

Variables	OR	95% CI	*p*
Duration of disease	3.414	3.008–3.858	0.024
EZ Integrity	2.816	2.293–3.545	0.016
logMAR BCVA	3.582	3.279–4.005	0.021
Outer HRF number	3.516	2.983–4.135	0.019
SII	2.975	2.307–3.624	0.012

EZ: elliptical zone; logMAR: logarithm of the minimum angle of resolution; BCVA: best-corrected visual acuity; HRF: hyperreflective retinal foci; SII: systemic immune-inflammatory index; OR: odds ratio; CI: confidence interval.

in the short term. In a prospective, randomized, double-blind, multicenter phase 3 clinical trial, where central macular thickness (CMT) and BCVA were primary outcome measures, ranibizumab injection showed effectiveness in improving visual acuity and reducing CMT [8]. Consistent with a previous study, our present investigation observed significantly lower CMT and higher BCVA at 1 and 3 months post-treatment compared to pre-treatment values.

Local and systemic inflammation contributes to RVO development by inducing atherosclerosis and systemic hypercoagulability. RVO is linked with atherosclerotic cardiovascular risk factors. Prior research has highlighted heightened expression of platelet-derived microvesicles and NETs-related markers in RVO patients, indicating functional activation of platelets and neutrophils [9]. RVO is influenced by the interplay of platelets, coagulation response, endothelial cells, and inflammatory response amidst blood flow abnormalities [10]. Investigations have explored the association between NLR, PLR and RVO, showing elevated NLR, PLR and MHR in RVO occurrence [11]. Timur *et al.* [12] reported that patients with higher SII had a significantly higher risk of ME. Therefore, understanding the link between inflammatory markers and RVO-ME could help clinicians in disease diagnosis and management. Studies indicate anti-VEGF therapy reduces inflammation in ME patients, potentially through ranibizumab's inhibition of leukocyte chemotaxis *via* VEGFR-1 and VEGFR-2 signaling, thereby suppressing various inflammatory factors [13]. Our investigations revealed reduced serum PLR, NLR and SII levels in male BRVO-ME patients following ranibizumab treatment, indicating decreased systemic inflammation associated with BRVO-ME in response to ranibizumab therapy.

Despite its safety and efficacy, ranibizumab treatment yields varied prognostic visual acuity outcomes among patients. A previous study reported significant reduction in CMT in over 90% of affected eyes after 6 months of ranibizumab treatment, yet BCVA recovery remained poor [14], indicating that while ME symptoms improved in most affected eyes post-treatment, some did not achieve the desired visual acuity levels. Therefore, investigating relevant factors that influence visual acuity prognosis post-ranibizumab treatment in BRVO-ME eyes could be of significant importance. Previous studies identified disease duration as an important predictor of visual acuity prognosis following treatment in BRVO-ME eyes [15]. Herein, our present study revealed that patients' eyes in the poor prognosis group exhibited significantly longer disease durations compared to those in the good prognosis group, thereby serving as an independent risk factor for visual prognosis after ranibizumab treatment in BRVO-ME eyes. We believe that this might be attributed to prolonged retinal and ME in eyes with longer disease duration, as prolonged edema can result in irreversible retinal damage [16] and more severe visual impairment, thereby increasing the likelihood of poor visual prognosis post-treatment. Another investigation revealed a correlation between poorer pre-treatment BCVA and worse visual recovery post-treatment [17]. Our results demonstrated that patients' eyes in the poor prognosis group had significantly lower pre-treatment BCVA compared to those in the good prognosis group and was an independent risk factor for BRVO-ME eye prognosis following ranibizumab treatment, indicating the importance of early intervention in BRVO-ME eyes during treatment to enhance BCVA for improved prognosis. Kim *et al.* [18] reported that ELM and EZ reflect the status and function of retinal photoreceptors and are closely correlated with BCVA recovery in affected eyes. Algahtani *et al.* [19] found that the integrity of the ELM and EZ was an important influence on the recovery of long-term vision in the affected eyes. Similarly, the results of our study showed that ELM integrity was an independent risk factor for visual prognosis in BRVO-ME eyes treated with ranibizumab, and no significant relationship was found between EZ and visual prognosis in BRVO-ME eyes. We hypothesized that this discrepancy may stem from the ability for EZ restoration on its own, contrasting with the irreparable nature of ELM damage, thereby underscoring the essential role of ELM in vision prognosis post-treatment. Furthermore, our study identified a higher number of outer layer HRFs in the poor prognosis group compared to the good prognosis group and identified outer layer HRFs as an independent risk factor for visual prognosis in BRVO-ME eyes treated with ranibizumab. This increase in HRFs likely accompanied the increase in hard exudates, resulting in more severe visual impairment and a poorer prognosis post-treatment. Additionally, serum SII levels were found to be significantly higher in the poor prognosis group compared to the good prognosis group and were an independent risk factor for poor visual acuity in BRVO-ME eyes treated with ranibizumab. We also observed that elevated SII levels corresponded to an increased inflammatory response and weakened immune response, indicative of a poor prognosis. This association likely stems from the systemic condition's impact on blood cell quantity and function [20], highlighting the potential of SII as a valuable biomarker for evaluating prognosis outcomes in BRVO-ME patients, offering promising insights for therapeutic interventions.

In addition to treating the eye condition, managing fundopathy involves assessing the patient's overall health status, which requires optimizing systemic risk factors in collaboration with relevant medical departments. The nomogram model facilitates the application of logistic regression findings for individual prognosis prediction, offering a visual representation conducive to clinical use. Widely employed in

oncology, nomograms are favored for evaluating cancer and medical prognoses [21]. In this study, we also developed a nomogram model based on independent risk factors for visual prognosis post-ranibizumab treatment in BRVO-ME eyes. Internal validation revealed a high C-index of 0.992 (95% CI: 0.983–1.001) for predicting visual acuity prognosis after ranibizumab treatment, with calibration curves demonstrating favorable observed versus predicted values. Moreover, the model's risk threshold for predicting poor prognosis could yield a net clinical benefit. Thus, the nomogram model exhibits high discrimination, accuracy, and clinical utility, serving as a valuable adjunctive predictive tool for visual acuity prognosis post-ranibizumab treatment in clinically affected BRVO-ME eyes.

This study had several limitations. Firstly, although the diabetic patients included in the sample did not exhibit signs of diabetic retinopathy, potential effects cannot be completely ruled out. Secondly, the scope of factors affecting visual recovery in this study was not exhaustive, warranting further investigation into the impact of other structures and parameters on visual prognosis. Additionally, while SII is easy to use and readily available, it is important to consider that the complete blood count can be influenced by factors such as medication, exercise status, and disease state. Therefore, its clinical application requires careful consideration. Further research is necessary to confirm the clinical usefulness of CBC-derived indicators like NLR, PLR and SII, among others, and to define appropriate reference ranges that accurately identify conditions with both good sensitivity and specificity. Furthermore, it is worth noting that this study focused on examining parameter changes in the male population, and differences between male and female populations remain to be clarified in future studies.

5. Conclusions

In summary, ranibizumab therapy for BRVO-ME demonstrated significant efficacy in improving both systemic inflammatory response and visual function, with a favorable safety profile. Several factors, including disease duration, baseline BCVA, pre-treatment ELM integrity, EZ integrity, and elevated blood SII, influenced the effective improvement of visual acuity in male patients with BRVO-ME. Furthermore, our proposed nomogram using OCT parameters and serum SII provides a valuable tool for prognostic evaluation of visual acuity following ranibizumab treatment in BRVO-ME-affected eyes.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

RYZ and WT—designed the study and carried them out; prepare the manuscript for publication and reviewed the draft of the manuscript. RYZ, FYH and LLF—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of The First People's Hospital of Zunyi (the Third Affiliated Hospital of Zunyi Medical University) (Approval no. 2018068). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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