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Correlation Between Characteristic OCT Biological Parameters and Prognosis After Conbercept Therapy for Macular Edema Secondary to Retinal Vein Occlusion

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Abstract: ***Objective:*** *To investigate the correlation between characteristic optical coherence tomography (OCT) biological parameters, TCED-HFV classification, and visual prognosis in patients with macular edema secondary to retinal vein occlusion (RVO-ME) after conbercept treatment, so as to provide evidence for clinical diagnosis and treatment.* ***Methods:*** *A total of 60 patients with RVO-ME were enrolled and divided into four groups (15 cases each) according to the TCED-HFV classification. All patients received intravitreal injection of conbercept combined with a treat-and-extend (T&E) regimen and were followed up for 6 months. Best-corrected visual acuity (BCVA), central retinal thickness (CRT), and key OCT parameters were measured before and after treatment, followed by statistical analysis.* ***Results:*** *There were no significant differences in general clinical data among the four groups (P>0.05). After treatment, BCVA was significantly improved and CRT was significantly decreased in all groups (all P<0.05). The early-stage group achieved the best post-treatment BCVA, while the atrophic stage group had the worst baseline BCVA but the largest amplitude of BCVA improvement. CRT was positively correlated with visual improvement; the integrity of the ellipsoid zone (EZ) and external limiting membrane (ELM) were key indicators for visual prognosis prediction; the severity of disorganization of the inner retinal layers (DRIL) and hyperreflective foci (HF) was negatively correlated with prognosis. The TCED-HFV classification could accurately reflect the disease stage and treatment response.* ***Conclusion:*** *The intravitreal conbercept injection combined with T&E regimen is safe and effective for RVO-ME. The TCED-HFV classification and related OCT parameters can effectively predict the prognosis of RVO-ME patients, and early intervention can better protect visual function.*

Keywords: RVO-ME, Conbercept, OCT Parameters, TCED-HFV Classification.

1. Introduction

Retinal vein occlusion (RVO) is one of the most common retinal vascular diseases, with an incidence rate of 0.3% to 0.6% [1]. Macular edema (ME) is a common complication of branch RVO (BRVO) and the main cause of visual impairment in RVO patients. Without timely intervention, it can lead to severe visual loss or even blindness. Vascular endothelial growth factor (VEGF) is a key effector molecule inducing ME. Intravitreal injection of anti-VEGF agents can effectively alleviate ME and improve visual acuity, which has become the first-line treatment for ME secondary to BRVO in clinical practice [2-3].

Conbercept is a recombinant anti-VEGF fusion protein that inhibits the binding of VEGF to its receptors, suppresses neovascularization, reduces vascular permeability, and regulates blood-retinal barrier permeability, thereby effectively preventing vascular leakage and inhibiting macular edema. The pathogenesis of RVO-ME is that venous occlusion increases retinal hydrostatic pressure and impairs vascular endothelial function, leading to disruption of the blood-retinal barrier and upregulation of various cytokines (including VEGF) in the eye. This results in leakage from intraretinal capillaries and fluid accumulation, ultimately forming ME [4]. Based on this pathophysiological mechanism, intravitreal anti-VEGF injection is recommended as the first-line treatment for RVO-ME [5-9].

At present, scholars worldwide have focused on OCT predictors of short-term visual prognosis in RVO-ME patients after anti-VEGF treatment, and it has been found that RVO patients with different morphological features on spectral-domain OCT (SD-OCT) scans have varying prognoses following anti-VEGF therapy [10]. Panozzo et al. [11] first applied the “TCED-HFV” assessment system to evaluate the prognosis of diabetic retinopathy-related macular edema. However, whether the TCED-HFV system is valuable for predicting the prognosis of RVO-ME remains to be further investigated.

RVO-ME is the most common cause of visual decline in affected patients. Recurrent macular edema can cause irreversible damage to retinal photoreceptors, severely affecting prognosis and even leading to blindness. Although intravitreal anti-VEGF injection is widely used as the first-line treatment for RVO-ME, its high cost imposes a heavy economic burden on patients. To reduce the cost and injection frequency of anti-VEGF therapy, the 3+PRN (pro re nata) or T&E regimen for RVO-ME has become a research hotspot [12-13]. Nevertheless, non-response or poor response to anti-VEGF agents is observed in some patients during follow-up. Therefore, predicting the efficacy of anti-VEGF treatment is a common concern for both patients and clinicians.

Four main parameters are evaluated on SD-OCT: central foveal thickness or macular volume, intraretinal cysts, the status of the ellipsoid zone (EZ) and external limiting membrane (ELM), and disorganization of the inner retinal layers (DRIL); three accompanying parameters include the number of hyperreflective foci (HF), subfoveal fluid, and

vitreoretinal relationship. Based on these parameters, RVO-ME is classified into four stages: early, progressive, severe, and atrophic maculopathy.

- **Early RVO-ME:** Central foveal thickness and/or macular volume increased by <30% above the maximum normal value (T1); small to moderate intraretinal cysts (C0–C1); identifiable and intact inner retinal layers, EZ, and ELM (E0, D0).

- **Progressive RVO-ME:** Central foveal thickness and/or macular volume increased by >30% above the maximum normal value (T1–T2); large intraretinal cysts with multiple cystic spaces (C1–C3); inner retinal layers still stratifiable (D0–D1); EZ and ELM damaged but visible (E0–E1).

- **Severe RVO-ME:** Central foveal thickness and/or macular volume increased by >30% above the maximum normal value (T1–T2); large intraretinal cysts with multiple cystic spaces (C1–C3); mostly disorganized inner retinal layers (D0–D1); EZ and ELM mostly invisible (E2).

- **Atrophic RVO-ME:** Decreased central foveal thickness and/or macular volume (T0); small intraretinal cystic spaces (C0–C2); complete destruction of inner retinal layers, EZ, and ELM (E2, D0–D1) [11].

The TCED-HFV assessment system was established to predict the therapeutic response to conbercept in RVO-ME patients.

2. Subjects and Methods

2.1 Study Subjects

This was a prospective observational study. Patients diagnosed with RVO-ME at the Department of Ophthalmology, Inner Mongolia Forestry General Hospital from October 1, 2023, to October 1, 2025, were enrolled. All patients voluntarily received intravitreal conbercept injection as anti-VEGF therapy. A central retinal thickness (CRT) >250 μm at the fovea was used as an indication for intravitreal anti-VEGF injection, and treatment decisions were fully respected by the patients. Regular anti-VEGF treatment was administered using the T&E regimen with scheduled follow-up.

This study was approved by the Ethics Committee of Inner Mongolia Forestry General Hospital (Ophthalmology Department) and complied with the principles of the Declaration of Helsinki. Complete medical records were available for all patients, including name, gender, age, and past medical history. Written informed consent was obtained from each patient before injection. All patients underwent standard distance visual acuity testing, non-contact intraocular pressure measurement, fundus photography, fluorescein angiography, and Heidelberg multi-wavelength laser SD-OCT scanning.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria

1) Unilateral ME secondary to RVO, with a normal contralateral eye;
2) Age ≥18 years;
3) SD-OCT examination showing CRT >250 μm and loss of normal foveal contour;
4) No prior anti-VEGF treatment;
5) Follow-up duration ≥6 months.

Exclusion criteria

1) Inability to complete all required examinations;
2) Refractive error >−6.0 D or >+3.0 D;
3) Poor fixation or severe media opacity preventing clear fundus imaging;
4) ME caused by other retinal diseases (e.g., diabetic retinopathy, age-related macular degeneration);
5) Previous fundus laser photocoagulation or intraocular surgery;
6) Poor-quality OCT images (signal strength <20 dB).

Retreatment criteria

1) BCVA decreased by >5 letters compared with the previous follow-up;
2) Active lesions persisted despite partial improvement after treatment;
3) Recurrent active lesions after initial improvement, with OCT showing intraretinal or subretinal fluid and retinal thickening >250 μm.

1.3 Ophthalmic Examinations

1) **Visual acuity:** Best-corrected visual acuity was measured using an international standard visual acuity chart and converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis.

2) **Refraction:** Refractive error was measured three times using an automatic computerized refractometer (NIDEK AOS-150, Japan) with the patient fixating on a flashing target. The patient closed their eyes for rest before and after each measurement.

3) **Intraocular pressure (IOP):** IOP was measured three times using a non-contact tonometer (NIDEK, Japan) with the patient fixating on a flashing target, and the average value was recorded.

4) **Color fundus photography (CFP):** 45° color fundus images centered on the fovea and optic disc were obtained by a skilled technician using a TRC-NW300 non-mydriatic fundus camera (Topcon, Japan).

5) **Spectral-domain optical coherence tomography (SD-OCT):** SD-OCT scanning of the affected eye was performed by an experienced ophthalmologist. The patient's forehead and chin were fixed on the headrest, and the eye was slightly adducted to fixate on the internal target. The scanner was aligned with the eye, and standard radial and linear scans of the macula were obtained. The SD-OCT system had a wavelength of 870 nm, scan depth of 1.9 mm, A-scan rate of

40,000 scans/s, and axial resolution of 3.8 μm. ETDRS macular thickness analysis was performed automatically. Ten retinal layers were clearly visualized on SD-OCT. The presence of DRIL, HF, EZ disruption, and ELM disruption was recorded in detail.

6) **DRIL:** Loss of clear boundaries between the ganglion cell-inner plexiform layer complex, inner nuclear layer, and outer plexiform layer on high-definition SD-OCT B-scans.

7) **HF:** Well-circumscribed, discrete, punctate hyperreflective foci with a diameter of >20 μm and <50 μm within the neurosensory retina, with reflectivity equal to or higher than that of the retinal pigment epithelium (RPE) on SD-OCT.

8) **ELM:** The first hyperreflective band representing the junctional complex between Müller glia and photoreceptors, visible as a continuous hyperreflective line between the outer nuclear layer and photoreceptor layer on OCT.

9) **EZ:** The hyperreflective band below the ELM, representing photoreceptor integrity, visible as a linear hyperreflective line at the inner-outer segment junction of photoreceptors on OCT.

10) **Treatment regimen (T&E group):** All patients received intravitreal injection of conbercept (2.5 mg) once a month. After 3 loading doses, patients were re-examined at 4-week intervals. If active lesions were present, injections were repeated, and follow-up was continued at 4-week intervals. If no active lesions were found, injections were still administered, and the follow-up interval was extended by 2 weeks (to 6 weeks). The follow-up interval was shortened to 4 weeks if active lesions were detected during follow-up, and extended by 2 weeks if no active lesions were found in consecutive visits. All patients were followed up for 6 months.

1.4 Surgical Procedure

Topical anesthesia was induced with oxybuprocaine hydrochloride eye drops. The surgical field was prepared and draped in a sterile manner. The conjunctival sac was irrigated with 1 mL of 5% povidone-iodine for 30 seconds, followed by normal saline irrigation to remove residual povidone-iodine. Using sterile technique, a 30-gauge needle connected to a 1-mL syringe was inserted 3.5–4.0 mm posterior to the limbus toward the center of the globe (avoiding horizontal insertion). Conbercept (0.05 mL, 2.5 mg) was slowly injected into the vitreous cavity. The needle was withdrawn gently, and the injection site was compressed with a sterile cotton swab for 1 minute. Tobramycin and dexamethasone ointment was applied to the conjunctival sac, and the eye was covered with a sterile dressing and eye pad.

1.5 Outcome Measures and Adverse Events

The primary outcome measure was the correlation between BCVA and TCED-HFV classification factors in the four groups during the 6-month follow-up. Secondary outcome measures included the number of conbercept injections and any recorded adverse events (e.g., intraocular inflammation, elevated IOP, retinal detachment).

1.6 Statistical Analysis

Statistical analysis was performed using SPSS 26.0 software (SPSS Inc., Chicago, USA). Normally distributed continuous data were presented as mean ± standard deviation (SD). The independent-samples t-test was used for between-group comparisons, and the paired t-test was used for pre- and post-treatment comparisons of the same group. Non-normally distributed continuous data were presented as median (interquartile range, P25, P75). The Mann–Whitney U test was used for between-group comparisons, and the Wilcoxon signed-rank test was used for pre- and post-treatment comparisons of the same group. Categorical data were presented as rates and analyzed using the chi-square test, adjusted chi-square test, or Fisher's exact test. Univariate and multivariate logistic regression analyses were used to identify factors associated with BCVA. A two-sided P value <0.05 was considered statistically significant.

3. Results

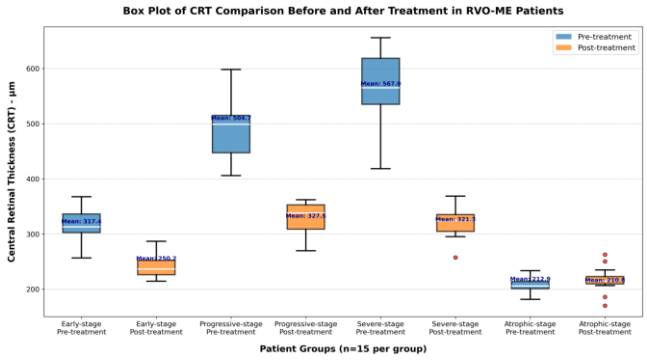
3.1 General Data

A total of 60 patients (60 eyes) were enrolled in this study, including 34 females (34 eyes) and 26 males (26 eyes). There were 15 patients in each of the early, progressive, severe, and atrophic RVO-ME groups. The mean ages of the four groups were 63.80 ± 11.28, 63.67 ± 7.18, 64.53 ± 12.37, and 68.07 ± 6.10 years, respectively. No significant differences in general clinical data (including age, gender, smoking status, hypertension, IOP, and eye side) were observed among the four groups (all P>0.05), indicating that the groups were comparable.

	Early-stage RVO-ME Group (n=15)	Progressive RVO-ME Group (n=15)	Severe RVO-ME Group (n=15)	Atrophic RVO-ME Group (n=15)	F	P
Age, years	63.80 ± 11.28	63.67±7.18	64.53 ± 12.37	68.07 ± 6.10	0.86	0.46
Gender, n(%)						
Male	7 (46.7)	6 (40.0)	6 (40.0)	7 (46.7)	-	-
Female	8 (53.3)	9 (60.0)	9 (60.0)	8 (53.3)	-	-
Initial CRT (μm)	317.40 ± 26.92	504.73 ± 74.26	567.00 ± 56.62	212.93 ± 13.71	279.02	0
Post-treatment CRT (μm)	250.20 ± 30.69	327.53 ± 170.0	321.33 ± 102.69	210.77 ± 11.64	8.78	0.0001
Initial BCVA (LogMAR)	0.66 ± 0.45	0.78 ± 0.42	0.85 ± 0.18	1.55 ± 0.22	11.32	0
Post-treatment BCVA (LogMAR)	0.21 ± 0.09	0.36 ± 0.37	0.37 ± 0.16	0.74 ± 0.20	11.24	0

	Early-stage RVO-ME Group (n=15)	Progressive RVO-ME Group (n=15)	Severe RVO-ME Group (n=15)	Atrophic RVO-ME Group (n=15)	F	P
Smoking, n (%)	5 (33.3)	7 (46.7)	7 (46.7)	10 (66.6)	χ^2=3.40	0.33
Hypertension, n(%)	10 (60.0)	10 (66.6)	12(75.0)	14 (93.3)	χ^2=4.10	0.25
Intraocular Pressure, mmHg	15.22±1.86	15.38±1.50	15.85±2.20	14.89±3.20	0.01	0.99
Eye Side, n(%)						
Left Eye	6 (40.0)	7 (46.7)	7 (46.7)	8 (53.3)	-	-
Right Eye	9 (60.0)	8 (53.3)	8 (53.3)	7 (46.7)	-	-

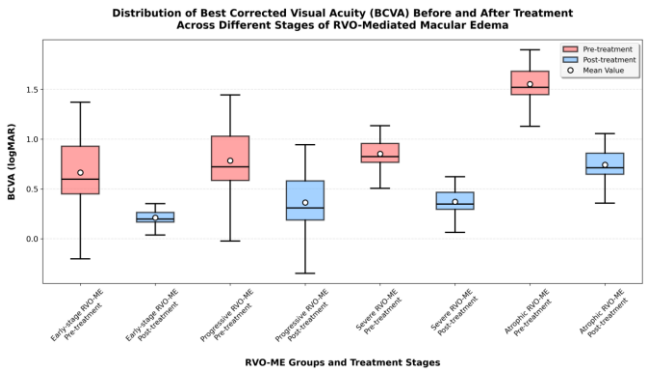
3.2 Central Retinal Thickness (CRT)



Baseline CRT showed a clear stage-dependent pattern: the severe group had the highest CRT, followed by the progressive, early, and atrophic groups (the latter was close to the normal range). After treatment, CRT decreased significantly in all groups except the atrophic group, with a narrower distribution, indicating consistent therapeutic efficacy of the regimen.

- **Early group:** Baseline CRT was 317.40 μm, which decreased to 250.20 μm after treatment, with a reduction of 67.20 μm (21.2%).
- **Progressive group:** Baseline CRT was 504.73 μm, which decreased to 327.53 μm after treatment, with a reduction of 177.20 μm (35.1%).
- **Severe group:** Baseline CRT was 567.00 μm, which decreased to 321.33 μm after treatment, with a reduction of 245.67 μm (43.3%), showing the largest reduction amplitude.
- **Atrophic group:** Baseline CRT was 212.93 μm, which decreased to 210.77 μm after treatment, with a reduction of 2.16 μm (1.0%), indicating a minimal therapeutic effect.

3.3 Best-Corrected Visual Acuity (BCVA, logMAR)



2.3.1 Overall Treatment Effectiveness

After treatment, BCVA was significantly improved (logMAR value significantly decreased) in all four groups, confirming that the T&E regimen combined with conbercept is effective across all stages of RVO-ME.

2.3.2 Efficacy Differences Among Stages

- **Atrophic group:** It had the greatest amplitude of BCVA improvement (baseline 1.55 ± 0.22, reduction of 0.81 logMAR), although it had the worst baseline vision.
- **Early group:** It achieved the best final BCVA (0.21 ± 0.09), indicating that early intervention can achieve optimal visual recovery.
- Disease severity was negatively correlated with baseline vision (the more advanced the stage, the worse the baseline vision), but all stages showed significant improvement after treatment, with no treatment failure cases.

3.4 Smoking and Hypertension

No significant differences in the prevalence of smoking or hypertension were found among the four groups (P>0.05). However, a numerical increasing trend was observed in the prevalence of these two factors with the progression of RVO-ME stages, suggesting that smoking and hypertension may be associated with the progression of RVO-ME. The high prevalence of smoking and hypertension in the atrophic group warrants attention as potential contributors or markers of advanced disease.

4. Conclusions

1) Conbercept treatment can significantly improve the outcomes of patients with all four stages of RVO-ME, confirming the effectiveness of anti-VEGF therapy and the necessity of active treatment for RVO-ME.

2) The early-stage RVO-ME group achieved the best therapeutic effect, highlighting the importance of early intervention.

3) Intravitreal conbercept injection combined with the T&E regimen is safe and effective for the treatment of RVO-ME. The TCED-HFV classification can accurately predict the treatment response and visual prognosis of RVO-ME patients.

5. Discussion

This study investigated the correlation between the TCED-HFV classification, OCT biological parameters, and visual prognosis in RVO-ME patients after conbercept anti-VEGF treatment. The results showed that conbercept was effective across all TCED-HFV stages, and early intervention yielded the best visual prognosis, which is consistent with the findings of mainstream domestic and international studies [14-16].

5.1 Effectiveness and Mechanism of Conbercept for RVO-ME

As a recombinant fusion-protein anti-VEGF agent, conbercept can potently block the binding of VEGF to its receptors, reduce retinal vascular permeability, and alleviate foveal fluid accumulation, thereby rapidly resolving macular edema and improving visual acuity. In this study, 60 patients treated with the standardized T&E regimen showed significant CRT reduction and BCVA improvement in all stages, which further validates that conbercept is a first-line therapy for RVO-ME.

The magnitude of edema reduction was the largest in the severe group (43.3%), followed by the progressive (35.1%) and early (21.2%) groups, indicating that greater baseline edema is associated with more prominent structural improvement after anti-VEGF treatment. The minimal CRT reduction in the atrophic group (1.0%) reflected that its pathology is dominated by retinal atrophy and photoreceptor damage rather than active vascular leakage, which further confirms that the TCED-HFV staging system can accurately reflect the pathophysiological characteristics of RVO-ME at different stages.

5.2 Prognostic Value of the TCED-HFV Classification

This study is the first to apply the TCED-HFV assessment system to predict the therapeutic outcomes of conbercept therapy for RVO-ME, and the results demonstrated a strong correlation between the TCED-HFV classification and treatment response:

1) **Early RVO-ME:** Patients in this stage have intact inner retinal layers and preserved EZ/ELM. After treatment, CRT rapidly returned to normal, and BCVA reached 0.21 ± 0.09, which was the best among all groups. This indicates that early intervention can maximally protect photoreceptor function and is a critical window for achieving optimal prognosis.

2) **Progressive and severe RVO-ME:** These two stages are characterized by large intraretinal cysts, DRIL, and damaged EZ/ELM. Although macular edema resolved substantially after treatment, visual recovery was inferior to that of the early group, indicating that irreversible structural damage limits the gain of visual function.

3) **Atrophic RVO-ME:** This stage is marked by retinal atrophy and complete disruption of EZ/ELM, with the worst baseline vision. Although visual acuity improved after treatment, it could not be restored to a favorable level, indicating that anti-VEGF therapy can only relieve symptoms once irreversible structural injury has occurred.

The TCED-HFV classification enables rapid OCT-based stratification of RVO-ME patients and precise prediction of their treatment response and visual outcomes, which is conducive to making individualized treatment decisions in clinical practice.

5.3 Prognostic Significance of Key OCT Parameters

- **CRT:** It is a core indicator of edema activity. The reduction of CRT after treatment was positively correlated with visual improvement, serving as a straightforward marker for evaluating therapeutic efficacy and guiding retreatment.
- **DRIL and HF:** These two parameters indicate inflammatory activity and ischemic injury in the retina. Greater severity of DRIL and higher number of HF were correlated with more injections and poorer visual prognosis.
- **EZ and ELM:** They are the strongest morphological predictors of final visual acuity. Better preservation of EZ and ELM was associated with better visual recovery, while complete disruption of EZ and ELM predicted irreversible vision loss.

Combining these key OCT parameters with the TCED-HFV staging system creates an integrated structure–function–prognosis assessment model, which is superior to the single use of CRT or visual acuity in predicting the prognosis of RVO-ME patients.

5.4 Clinical Applicability of the T&E Regimen

The T&E regimen, based on the 3+PRN regimen, allows flexible extension of follow-up intervals according to the activity of retinal lesions while maintaining effective control of macular edema and improvement of visual acuity. This regimen can reduce the frequency of injections, lower medical costs, and reduce the risk of complications related to intravitreal injection. All stages of RVO-ME patients benefited from this strategy, making the T&E regimen the preferred follow-up protocol for conbercept-treated RVO-ME, which is suitable for widespread application in primary and general hospitals.

5.5 Risk Factors and Clinical Implications

Although there were no significant differences in the prevalence of hypertension and smoking among the four groups, their prevalence showed an upward trend with the progression of RVO-ME stages, suggesting that these two factors may accelerate the progression of RVO-ME to the atrophic stage. Therefore, in clinical management, while administering anti-VEGF therapy, attention should be paid to the control of systemic risk factors (such as hypertension and smoking) to slow down the deterioration of RVO-ME.

5.6 Study Limitations

1) This study had a limited sample size and adopted a

single-center observational design, so the results need to be validated by multicenter, large-sample prospective studies.

2) The follow-up duration was 6 months, which is relatively short, and long-term (≥1 year) data on the stability of visual function and retinal structure are lacking.

3) No subgroup analysis was performed for branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO), so potential differences in therapeutic efficacy between the two subtypes were not evaluated.

5.7 Summary

Intravitreal conbercept injection combined with the T&E regimen is safe and effective for the treatment of RVO-ME. The TCED-HFV classification can accurately predict the treatment response and visual prognosis of RVO-ME patients. Early diagnosis and anti-VEGF intervention are essential to maximize the protection of retinal structure and visual function. The combined assessment using key OCT parameters (CRT, DRIL, EZ/ELM, HF) and the TCED-HFV staging system provides reliable guidance for individualized treatment and follow-up of RVO-ME patients.

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