Effect of Intravitreal Corticosteroid on DRIL Regression and Visual Outcomes in Retinal Vein Occlusion

Efeito do Corticosteroide Intravítreo na Regressão do DRIL e nos Resultados Visuais nas Oclusões Venosas da Retina

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ABSTRACT

INTRODUCTION: Retinal vein occlusion (RVO) is a common cause of sudden, painless visual loss, usually due to macular edema. Disorganization of the retinal inner layers (DRIL) is a key optical coherence tomography (OCT) biomarker of visual prognosis, but data on its response to corticosteroid therapy in RVO are limited. This study evaluated the short-term effects of intravitreal injection (IVI) of corticosteroids on DRIL and other OCT biomarkers, and their associations with visual and anatomical outcomes.

METHODS: This retrospective study included eyes with macular edema secondary to central or branch RVO that received a single corticosteroid IVI (triamcinolone, dexamethasone, or fluocinolone acetonide), between January 2018 and December 2024. OCT and clinical evaluations were performed at baseline and 3 months. Images were independently graded by two masked ophthalmologists (agreement 89.8%). DRIL was graded (0-3) according to the number of retinal layers involved and classified by foveal or parafoveal location. Changes in best-corrected visual acuity (BCVA) and central macular thickness (CMT) were analyzed using paired tests. Correlations were evaluated using Spearman's coefficient (ϱ), and multivariable regression identified predictors of final BCVA.

RESULTS: Eighty-three eyes from 83 patients (mean age, 73.4 ± 9.8 years) were included. Median BCVA improved from 0.48 to 0.40 logMAR (p=0.015) and CMT decreased from 447 to 314 µm (<0.001), after corticosteroid IVI. DRIL regressed in 21.3% of eyes with foveal DRIL, decreasing from 85.5% to 71.1% (p=0.012). Final BCVA correlated with DRIL grade (ϱ=0.41, p<0.001) and CMT (ϱ=0.24, p=0.033). In multivariate regression analysis (R^2=0.231, p<0.001), DRIL persistence, residual CMT and intraretinal cysts independently predicted poorer BCVA. Treatment-naïve eyes showed greater CMT reduction (p=0.025) and DRIL regression (57.1% *vs* 17.6%; p=0.034). Eyes with baseline DRIL had poorer final BCVA (0.40 *vs* 0.15 logMAR; p=0.025).

CONCLUSION: Intravitreal corticosteroid therapy provides early anatomical and functional improvement in RVO and promotes regression of retinal disorganization. Persistent DRIL and residual edema independently predict poorer visual outcomes, confirming DRIL as a clinically relevant OCT biomarker beyond macular thickness measures. Earlier corticosteroid use may favour structural reorganization, warranting prospective confirmation.

KEYWORDS: Biomarkers; Glucocorticoids/therapeutic use; Intravitreal Injections; Macular Edema; Retinal Vein Occlusion/drug therapy; Tomography, Optical Coherence; Visual Acuity.

RESUMO

INTRODUÇÃO: A oclusão venosa da retina (OVR) é uma das principais causas de hipovisão súbita e indolor, geralmente associada a edema macular. A desorganização das camadas internas da retina (DRIL) é um biomarcador de tomografia de coerência ótica (OCT) com relevância prognóstica para a função visual, embora existam poucos dados sobre a sua resposta ao tratamento com corticosteroides na OVR. Este estudo avaliou o efeito a curto prazo da injeção intravítrea (IIV) de corticosteroide sobre o DRIL e a sua relação com os resultados anatómicos e visuais.

MÉTODOS: Estudo retrospetivo que incluiu olhos com edema macular secundário a OVR, tratados com uma única IIV de corticosteroides, entre janeiro de 2018 e dezembro de 2024. As avaliações clínicas e de OCT foram realizadas na baseline e aos 3 meses de seguimento. As imagens foram analisadas de forma independente por dois oftalmologistas. O DRIL foi categorizado (0–3) de acordo com o número de camadas envolvidas. As variações da melhor acuidade visual corrigida (MAVC) e da espessura macular central (EMC) foram analisadas com testes emparelhados.

RESULTADOS: Foram incluídos 83 olhos de 83 doentes (idade média 73,4 ± 9,8 anos). A mediana da MAVC melhorou de 0,48 para 0,40 logMAR (p=0,015) e a EMC diminuiu de 447 para 314 µm (p<0,001) após a IIV. O DRIL regrediu em 21,3% dos olhos, com redução da sua presença foveal de 85,5% para 71,1% (p=0,012). A MAVC final correlacionou-se com o grau de DRIL (coeficiente de Spearman, ϱ=0,41; p<0,001) e com a EMC (ϱ=0,24; p=0,033). Na regressão multivariada (R^2 = 0,231; p<0,001), a persistência de DRIL, a EMC residual e os quistos intrarretinianos foram preditores independentes de pior MAVC.

CONCLUSÃO: A terapêutica intravítrea com corticosteroide proporciona melhoria anatómica e funcional precoce na OVR e promove a regressão do DRIL. A persistência de DRIL e o edema residual associam-se a piores resultados visuais, reforçando o seu papel como biomarcador de OCT. A introdução mais precoce de corticosteroides poderá favorecer a reorganização estrutural da retina, devendo estes achados ser confirmados em estudos prospetivos.

PALAVRAS-CHAVE: Acuidade Visual; Biomarcadores; Edema Macular; Glucocorticoides/uso terapêutico; Injeções intravítreas; Oclusão da Veia Retiniana/tratamento farmacológico; Tomografia de Coerência Óptica.

INTRODUCTION

Retinal vein occlusion (RVO) is a major cause of sudden, painless visual loss, most commonly due to macular edema secondary to vascular obstruction.[1] RVOs are classified as central (CRVO), hemi-, or branch retinal vein occlusions (BRVO), with BRVO being the most frequent subtype.[2] Venous blockage caused by thrombus formation results in retinal venous dilation and congestion, intraretinal hemorrhages, ischemia, and macular edema, ultimately leading to progressive or even sudden loss of visual acuity when the foveal region is affected.[3]

The main treatment options include intravitreal injections (IVI) of anti–vascular endothelial growth factor (anti-VEGF) agents and corticosteroids, and, in specific cases, laser therapy.[4] Intravitreal corticosteroids such as triamcinolone, dexamethasone, and fluocinolone acetonide are particularly effective in reducing capillary permeability and inflammatory mediators involved in macular edema, leading to improved visual outcomes after treatment.[5,6] Steroids reduce macular edema by inhibiting multiple inflammatory mediators (in addition to VEGF), stabilizing the blood–retina barrier, and decreasing vascular permeability and tissue edema.[7] Their use is especially indicated when inflammation plays a major role in macular edema.[5] Early initiation of corticosteroid therapy may also be advantageous, as prompt suppression of the inflammatory cascade can prevent chronic macular damage and enhance functional recovery.[4]

Several optical coherence tomography (OCT) biomarkers have been identified as predictors of visual prognosis following treatment.[8] One of the most relevant is the disorganization of the retinal inner layers (DRIL), characterized by loss of distinction between the inner retinal boundaries.[9] In the context of RVO, some studies have reported that the absence of DRIL prior to initiating anti-VEGF treatment is associated with better visual acuity at six months, whereas its persistence during therapy correlates with poorer visual prognosis.[10] Thus, DRIL should be considered an OCT biomarker associated with visual prognosis in RVO.

Intravitreal dexamethasone implants have emerged as a promising therapeutic alternative, however, data regarding their impact on DRIL remain limited. Castro-Navarro *et al* found no significant relationship between OCT biomarkers (including DRIL) at baseline and after dexamethasone implant treatment, possibly due to the small sample size[1]. Moreover, that study only assessed the presence or absence of DRIL, without quantifying its extent. Conversely, Horozoglu *et al* suggested that worsening of DRIL following treatment for refractory macular edema could explain the lack of functional improvement despite reduced central foveal thickness.[11] However, these conclusions were not restricted to specific etiologies such as RVO.

Furthermore, little is known about the influence of the timing of corticosteroid introduction, whether in treatment-naïve or previously treated eyes, on DRIL evolution. The impact of early versus delayed corticosteroid use on retinal structural recovery, therefore remains poorly understood.

This study aimed to evaluate the effect of intravitreal corticosteroids on DRIL and other OCT biomarkers, and to assess their relationship with visual and anatomical outcomes in eyes with RVO.

METHODS

STUDY DESIGN

This retrospective observational single-center study was conducted at the Ophthalmology Department of the Unidade Local de Saúde de Entre o Douro e Vouga, Portugal. All data were anonymized. The study followed the principles of the Declaration of Helsinki for research involving human subjects and was approved by the Ethics Committee of ULS Entre Douro e Vouga (approval number: CES n.º 46/2025). Owing to the retrospective design and absence of patient-identifying information, the requirement for informed consent was waived.

PARTICIPANTS

Patients aged ≥18 years diagnosed with macular edema secondary to central or branch RVO who received a single corticosteroid IVI were included. Both treatment-naïve eyes and eyes previously treated with anti-vascular endothelial growth factor (anti-VEGF) agents were eligible. Eligible patients had complete ophthalmologic and imaging evaluations at baseline and approximately 3 months after treatment. The study period extended from January 2018 to December 2024.

Exclusion criteria included follow-up longer than 4 months after IVI, significant media opacities precluding high-quality OCT imaging, and coexisting retinal diseases potentially affecting visual or structural outcomes, such as age-related macular degeneration or diabetic retinopathy. Patients with missing OCT data or incomplete clinical records were also excluded.

IMAGING AND MEASUREMENTS

All eyes underwent comprehensive ophthalmologic examination, including best-corrected visual acuity (BCVA) assessment and macular OCT scans at baseline and follow-up. BCVA was converted to logarithm of the minimum angle of resolution (logMAR) for statistical analysis. BCVA was also expressed in ETDRS letter equivalents for descriptive purposes. OCT examinations were performed using the Spectralis 2 ® HRA+OCT device (Heidelberg Engineering, Heidelberg, Germany) in infrared and OCT combined mode.

OCT EXAMINATION AND GRADING

All patients had macular scans centered on the fovea. The acquisition protocol was a 20º × 20º macular cube in high-resolution mode. Only images with a signal strength >20 dB were analyzed. The central 1 mm (foveal) and parafoveal areas (1–3 mm) were evaluated according to the 1-3-6 mm ETDRS grid centered on the fovea, as described by Vujosevic *et al*.[12] Three horizontal B-scans were analyzed: the foveal center, the one immediately above, and the one immediately below. Fig. 1 illustrates the OCT marking procedure used to define the limits of the foveal and parafoveal evaluation areas.

The central macular thickness (CMT) was automatically obtained from the foveal-centered OCT scan and expressed in micrometers (μm). *Minor* manual corrections of the automated segmentation were made by a senior grader before grading. DRIL was defined as previously described and classified according to the retinal layers involved.[12] In this study, the term DRIL/DROL was used to describe a spectrum of retinal disorganization, graded from 0 to 3 ac-

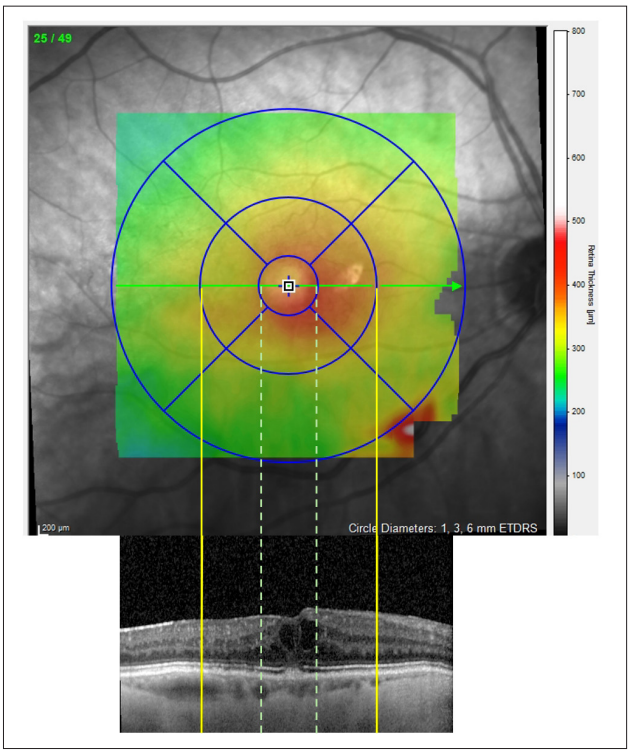

Figure 1. Example of OCT grading showing manual boundaries for foveal (central 1 mm) and parafoveal (1–3 mm) assessment used for DRIL and ancillary biomarkers.

cording to the extent of involvement of the inner and outer retinal layers, as detailed below:

- Grade 1 (DRIL): involving the ganglion cell layer, inner plexiform layer (IPL), inner nuclear layer (INL), and outer plexiform layer (OPL);
- Grade 2 (disorganization of the retinal outer layers - DROL): grade 1 plus involvement of the outer nuclear layer;
- Grade 3 (DROL-plus): grade 2 plus ellipsoid zone (EZ) or external limiting membrane (ELM) interruption.

For clarity, "DRIL" specifically refers to grade 1 (inner retinal involvement), whereas higher grades (DROL and DROL-plus) reflect additional outer retinal disruption. For each case, the presence or absence of retinal disorganization was recorded, even when incomplete. DRIL/DROL extension was categorized as foveal, parafoveal, or both. Additional structural parameters included the presence of neurosensory detachment, subfoveal EZ (1 mm) and ELM integrity, subfoveal hyperreflective material, and intraretinal cysts. The cysts were classified by shape (regular vs irregular) and location (inner, outer, or both layers).

All OCT images were evaluated independently by two ophthalmologists (PCT and LD), with discrepancies resolved by consensus discussion. Intergrader agreement was 89.8%, ensuring consistent and reproducible grading.

TREATMENT

All patients received a single intravitreal corticosteroid injection, either triamcinolone acetonide, dexamethasone implant (Ozurdex®; AbbVie) or fluocinolone acetonide (Iluvien®, Alimera) according to physician discretion. None of the included eyes had received prior corticosteroid treatment. The number of previous anti-VEGF injections, when applicable, was recorded. No additional treatment was administered during the 3-month observation period.

STATISTICAL ANALYSIS

Demographic and baseline ocular characteristics were summarized using traditional descriptive methods. Non-normally distributed variables were expressed as medians with interquartile ranges, and categorical data as frequencies and percentages.

Comparisons between baseline and post-treatment values were performed using paired statistical tests. DRIL regression was analyzed only among eyes presenting measurable DRIL at baseline. Correlations between functional and structural parameters were assessed using Spearman's rank correlation coefficient (ϱ), given the non-normal distribution of the data.

Changes in functional and anatomical parameters were expressed as deltas (Δ), calculated as the difference between post-treatment and baseline values (Δ = post-treatment – baseline). Changes in ordinal variables were analyzed using the Wilcoxon signed-rank test. Subgroup analyses comparing treatment-naïve and previously treated eyes were performed using Mann–Whitney U test for continuous non-parametric data, the Student's t-test for normally distributed variables, and Fisher's exact test for categorical data.

Variables identified as significant predictors of final BCVA in univariate analysis were included in a multivariable linear regression model to assess their independent effects on final BCVA. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30.

RESULTS

A total of 134 eyes were initially selected. Twenty-three eyes were excluded due to missing data, 11 did not attend the follow-up visit within the predefined post-injection period, 9 were lost to follow-up, and 8 were excluded because of concomitant retinal pathologies. Consequently, 83 eyes (of 83 patients) were included in the final analysis.

DEMOGRAPHIC AND OCULAR CHARACTERISTICS

The mean age was 73.4 ± 9.8 years, and 54.2% were female. The mean follow-up period was 2.63±1.12 months. Seven eyes (8.4%) were treatment-naïve, while the remaining eyes had previously received intravitreal injections, with a median of 6 (IQR 4-8) prior IVI. The median interval between the last anti-VEGF injection and corticosteroid administration was 92 days (IQR, 66–165.5). Comorbidities included diabetes mellitus in 21.7% and systemic hypertension in 69.7% of patients. A total of 72.3% of eyes were phakic at baseline. At baseline, 41% of eyes had CRVO and 59% BRVO. Baseline characteristics are summarized in Table 1.

BASELINE DATA

At baseline, the median BCVA was 0.48 logMAR (IQR, 0.30–1.00) and the mean IOP was 13.8 ± 2.4 mmHg. The median CMT measured 447 μm (IQR, 313–571). DRIL was present in 85.5% of eyes in the foveal region and 84.3% in the parafoveal area. Based on the DRIL/DROL classification, 9.6% of eyes showed no disorganization, 6.0% were classified as grade 1 (DRIL), 28.9% as grade 2 (DROL), and 55.4% as grade 3 (DROL plus). Detailed baseline structural parameters are summarized in Table 2.

CLINICAL OUTCOMES AFTER CORTICOSTEROID TREATMENT

After corticosteroid injection, there was a significant improvement in functional and anatomical parameters. Median BCVA improved to 0.40 logMAR (IQR, 0.18–0.90), equivalent to approximately 65 ETDRS letters, representing an increase of +4 letters (p=0.015). Mean IOP increased to 16.6 ± 5.2 mmHg (p<0.001). CMT decreased significantly to 314 μm (IQR, 259–454), corresponding to a mean reduction of −133 μm (p<0.001).

Structurally, there was a regression of DRIL/DROL grade following treatment in 21.3% of the eyes. The proportion of eyes with foveal DRIL decreased from 85.5% to 71.1% (p=0.012), and parafoveal DRIL decreased from 84.3% to 71.1% (p=0.003). The distribution of DRIL/DROL grades also shifted significantly toward milder disorganization, with an increase in eyes classified as grade 0 (from 9.6% to 20.0%) and a reduction in higher grades (Wilcoxon signed-

Table 1. Baseline demographic and clinical characteristics of the study sample (n=83).

Variables	Value (n = 83)
Age (y), mean ± SD	73.4 ± 9.8
Gender, female, n (%)	45 (54.2)
Study eye, n (%)	
Right	43 (51.8)
Left	40 (48.2)
Follow-up duration (months), mean ± SD	2.63 ± 1.12
Systemic comorbidities, n (%)	
Diabetes *mellitus*	18 (21.7)
Systemic hypertension	58 (69.7)
Lens status, phakic (%)	60 (72.3)
Type of retinal vein occlusion, n (%)	
CRVO	34 (41.0)
BRVO	49 (59.0)
Previous IVI use, n (%)	
Yes	76 (91.6)
No (treatment-naïve)	7 (8.4)
Previously treated eyes, median number of prior IVI (IQR)	6 (4–8)
BCVA (logMAR), median [IQR]	0.48 [0.30–1.00]
CMT (µm), median [IQR]	447 [313–571]
IOP (mmHg), mean ± SD	13.8 ± 2.4
IVI corticosteroid, n (%)	
Triamcinolone	74 (89.2)
Dexamethasone	8 (9.6)
Fluocinolone Acetonide	1 (1.2)

SD, standard deviation; IQR, interquartile range; IVI, intravitreal injection; BCVA, best-corrected visual acuity; CMT, central macular thickness; IOP, intraocular pressure; CRVO, central retinal vein occlusion; BRVO, branch retinal vein occlusion.

rank test, p=0.030). No statistically significant changes were observed in EZ or ELM integrity, neurosensory detachment, or subfoveal hyperreflective material. Intraretinal cysts were found in 75.7% of eyes at baseline and in 59.0% at 3 months, representing a significant reduction (p<0.001).

CORRELATION ANALYSIS

Correlation analysis revealed significant associations between visual and structural parameters. BCVA correlated positively with final DRIL/DROL grade (ϱ=0.41, p<0.001), CMT (ϱ = 0.24, p=0.033), EZ disruption (ϱ = 0.45, p<0.001), and ELM alteration (ϱ=0.39, p<0.001). CMT correlated moderately with DRIL/DROL grade (ϱ=0.41, p<0.001), and DRIL/DROL showed strong correlations with EZ disruption (ϱ=0.89, p<0.001) and ELM (ϱ=0.80, p<0.001) integrity. Among temporal changes, ΔBCVA correlated with ΔCMT (ϱ=0.33, p=0.002) and ΔCMT correlated with ΔDRIL (ϱ=0.43, p<0.001), while the relationship between ΔDRIL and ΔBCVA did not reach statistical significance (p=0.21).

In the final regression model (Table 3) including structural parameters at 3 months (R^2 = 0.231, p<0.001), final BCVA was significantly influenced by the persistence of retinal disorganization (β = 0.42, p<0.001), residual CMT (β = 0.36, p=0.005), and the absence of intraretinal cysts (β = −0.37, p=0.008).

SUBGROUP ANALYSIS

Effect of treatment- naïve status

The median CMT reduction was higher in the naïve group than in pretreated eyes (p=0.025). DRIL/DROL regression occurred in 57.1% of naïve eyes and 17.6% of pretreated eyes (p=0.034). No significant differences were found between groups regarding EZ disruption, ELM alteration or subfoveal hyperreflective material. Detailed data are presented in Table 4.

Effect of baseline DRIL/DROL presence on outcomes

Median CMT was 464 µm (IQR, 350–630) in eyes with DRIL/DROL versus 259 µm (IQR, 224–290) in eyes without retinal disorganization (p=0.048). Median final BCVA was 0.40 logMAR (IQR, 0.18–1.00) in eyes with baseline DRIL/DROL compared with 0.15 logMAR (IQR, 0.00–0.48) in eyes without retinal disorganization (p=0.025).

DISCUSSION

In this study, we evaluated early functional and structural outcomes after a single intravitreal corticosteroid injection in eyes with RVO. Significant reductions in macular thickness and BCVA gain were observed, accompanied by notable regression of retinal disorganization. Importantly, eyes with persistent DRIL/DROL at 3 months exhibited poorer visual outcomes, highlighting the clinical relevance of this OCT biomarker in the assessment of therapeutic response.

The definition of DRIL has evolved over time. Initially, it referred exclusively to the loss of distinction within the inner retinal layers, but more recent studies have expanded this concept to include broader retinal disorganization, now described as DROL.[10,13] In our study, we adopted a comprehensive grading system of retinal disorganization, inspired by previous classifications, that accounts for both inner and outer retinal integrity.[12] This approach allowed a more detailed assessment of the relative contribution of each retinal layer to functional outcomes in RVO. To our knowledge, this is the first study to apply such an extended DRIL/DROL grading scale to retinal vein occlusion. We demonstrated that corticosteroid therapy effectively reduced both the grade and the extent of retinal disorganization in the foveal and parafoveal regions after 3 months, further emphasizing the value of this OCT biomarker in the structural evaluation of RVO.

DRIL has been consistently reported as a relevant biomarker of visual prognosis in retinal vascular diseases. Chan *et al*. demonstrated that early DRIL recovery at three months may serve as a predictive factor for favorable visual outcomes.[14] Our results demonstrated a strong association between DRIL/DROL grade and final BCVA,

Table 2. Comparison of functional and structural parameters at baseline and 3 months after intravitreal corticosteroid injection. Significant *p*-values (<0.05) are marked with an asterisk.

Parameter	Baseline	3 months	Change (Δ)	*p*-value
Functional outcomes				
BCVA (logMAR), median [IQR]	0.48 [0.30-1.00]	0.40 [0.18-0.90]	-0.08	**0.015***
BCVA (ETDRS letters), median [IQR]	61 [35–70]	65 [40–72]	+4 letters	—
IOP (mmHg), mean ± SD	13.8 ± 2.4	16.6 ± 5.2	+2.8	**<0.001***
Structural outcomes				
CMT (μm), median [IQR]	447 (313–571)	314 (259–454)	−133	**<0.001***
Presence of DRIL, (%)				
Foveal DRIL	85.5	71.1	↓	**0.012***
Parafoveal DRIL	84.3	71.1	↓	**0.003***
DRIL/DROL grade, (%)				**0.030***
Grade 0 (None)	9.6	20.5	↑	
Grade 1 (DRIL)	6.0	4.8	↓	
Grade 2 (DROL)	28.9	22.9	↓	
Grade 3 (DROL plus)	55.4	51.8	↓	
EZ disruption, (%)	56.6	54.2	—	0.774
ELM alteration, (%)	37.8	43.4	—	0.267
Subfoveal hyperreflective material (%)	38.3	34.9	—	0.664
Neurosensory detachment (%)	20.5	10.8	↓	0.115
Intraretinal cysts (present) (%)	75.7	59.0	↓	**<0.001***
Regularity (only when cysts present)				0.453
Regular	24.3	22.4	—	
Irregular	75.7	77.6	—	
Extension (only when cysts present)				0.445
Inner	7.1	16.3	↑	
Outer	5.7	2.0	↓	
Both	87.1	81.6	—	

BCVA, best-corrected visual acuity; CMT, central macular thickness; IOP, intraocular pressure; DRIL, disorganization of the retinal inner layers; DROL, disorganization of the retinal outer layers; EZ, ellipsoid zone; ELM, external limiting membrane; IQR, interquartile range.

Table 3. Multiple linear regression analysis for predictors of final best-corrected visual acuity. Higher DRIL/DROL grade and CMT were independently associated with poorer vision, whereas the absence of intraretinal cysts was correlated with better BCVA.

Variable	Unstandardized coefficient (B)	Standardized coefficient (β)	t	*p*-value
Final BCVA as dependent variable ($R^2 = 0.231$, $p < 0.001$)				
DRIL/DROL grade at 3 months	0.197	0.419	3.490	**<0.001***
CMT at 3 months (μm)	0.001	0.362	2.888	**0.005***
Intraretinal cysts at 3 months	−0.419	−0.373	−2.704	**0.008***
Constant	−0.018	—	−0.121	0.904

BCVA, best-corrected visual acuity; CMT, central macular thickness; DRIL, disorganization of the retinal inner layers; DROL, disorganization of the retinal outer layers.

supporting the role of retinal organization as a determinant of visual potential. This relationship likely reflects disruption of the inner retinal neuronal network, since disorganization or loss of bipolar and Müller cells impairs signal transmission from photoreceptors to ganglion cells.[12,15,16] Electrophysiologic studies have shown reduced P1 amplitude and delayed implicit time in eyes with DRIL or cystic changes, supporting the presence of functional disturbance within these retinal circuits.[17] Furthermore, the coexistence of DRIL and EZ disruption has been shown to have an additive detrimental effect on visual function.[18] These mechanisms help explain why eyes with persistent retinal disorganization maintained worse visual acuity despite anatomical improvement.

Interestingly, recent evidence has linked DRIL to retinal inflammation. Midena *et al* correlated DRIL with higher aqueous levels of glial fibrillary acidic protein, a biomarker of Müller cell activation, suggesting that this OCT bio-

Table 4. Comparison of functional and structural outcomes between treatment-naïve and previously treated eyes at 3 months after intravitreal corticosteroid injection.

Parameter	Naïve eyes (n = 7)	Previously treated eyes (n = 76)	*p*-value
ΔBCVA (logMAR), median [IQR]	−0.18 [−0.30, 0]	−0.05 [−0.20, 0.09]	0.430
CMT (μm), median [IQR]	-182 (-510, -153)	-45 (-206, -31)	**0.025***
DRIL regression (%)	57.1 %	17.6 %	**0.034***
EZ disruption at 3 months (%)	42.9	55.3	0.697
ELM alteration at 3 months (%)	28.6	44.7	0.693
Subfoveal hyperreflective material at 3 months (%)	42.9	34.2	0.691
Intraretinal cysts at 3 months (%)	28.6	61.8	0.117

BCVA, best-corrected visual acuity; CMT, central macular thickness; DRIL, disorganization of the retinal inner layers; DROL, disorganization of the retinal outer layers; EZ, ellipsoid zone; ELM, external limiting membrane; IQR, interquartile range.

marker reflects glial dysfunction rather than solely structural disorganization.[16] Although this relationship was described in diabetic macular edema, it supports the notion that DRIL may represent an imaging expression of inner retinal inflammation, a mechanism also relevant in retinal vein occlusions and potentially modulated by corticosteroid therapy.

The strong interdependence observed between DRIL/DROL, EZ, and ELM alterations indicates that inner retinal damage often coexists with outer retinal disruption, reinforcing the concept of global retinal remodeling in chronic edema. Thus, a higher DRIL/DROL grade may serve as a more comprehensive biomarker integrating both inner and outer retinal disorganization.

In our multivariate model, the influence of DRIL/DROL on visual function was independent of CMT, emphasizing that structural restoration of the inner retina, rather than edema resolution alone, is critical for functional gain. This underscores the clinical observation that macular edema reduction does not necessarily translate into visual recovery if neuronal disorganization persists.

Recent literature suggests that persistent macular edema in RVO frequently stems from inflammatory mechanisms rather than VEGF overexpression alone.[4] Consequently, switching to corticosteroid therapy is generally considered when CMT remains above 275–300 μm after three to six anti-VEGF injections. In our series, the median number of prior injections before switching was slightly higher, likely reflecting real-world delays and stepwise treatment approaches within public healthcare settings.

Subgroup analysis showed that treatment-naïve eyes experienced greater anatomical and structural improvements, including a higher rate of DRIL/DROL regression, compared with previously treated eyes. Although this subgroup was small, the trend supports the hypothesis that early corticosteroid administration may favor retinal reorganization and functional recovery. Further prospective studies, ideally randomized controlled trials, are warranted to explore this question.

The presence of retinal disorganization at baseline was associated with greater macular thickening and poorer visual outcomes, suggesting that early inner retinal disorganization reflects more severe structural damage and limited recovery potential. Previous studies have also reported that baseline DRIL may predict a reduced therapeutic response in retinal vein occlusion, consistent with our findings.[10,19] Although only a small number of eyes were free of retinal disorganization at presentation, these eyes achieved better anatomical and functional outcomes, supporting prior evidence that baseline DRIL acts as a prognostic marker of irreversible neuronal injury.

The strengths of this study include detailed OCT biomarker grading and a focus on early corticosteroid outcomes in RVO, providing real-world evidence on short-term structural and functional responses. Limitations include its retrospective design, short follow-up period, and the use of different corticosteroid agents, which may limit generalizability to other settings. However, the vast majority of eyes were treated with triamcinolone as the first-line intravitreal corticosteroid in our center, reflecting real-world practice. In addition, the high proportion of phakic eyes may have influenced visual acuity outcomes, as early corticosteroid-induced lens opacities may have slightly underestimated visual improvement. Nevertheless, these results reflect actual clinical practice in our setting. Future studies with longer follow-up are needed to determine whether regression of retinal disorganization predicts durable functional recovery and to clarify the long-term effects of different corticosteroid agents.

CLINICAL IMPLICATIONS

Assessment of retinal disorganization provides a complementary and functionally relevant metric for monitoring RVO. In clinical practice, eyes with persistent DRIL/DROL despite edema reduction may require closer follow-up or combined therapy strategies, as structural disorganization may precede functional decline.

CONCLUSION

In conclusion, our findings confirm the short-term efficacy of corticosteroid therapy in RVO and reinforce the importance of DRIL as a structural biomarker of visual prognosis. While CMT reduction reflects edema control, DRIL/DROL more accurately represents the functional integrity of the retinal neural network. Assessment of retinal disorganization should therefore complement conventional OCT metrics when monitoring response to treatment and predicting visual outcomes.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

PCT and LD: Conceived the study, collected and analyzed the data, and contributed to writing and revising the manuscript.

MG, JAA, and JCP: Contributed to data interpretation, manuscript writing, and critical review.

All authors approved the final version to be published.

PCT e LD: Conceberam o estudo, recolheram e analisaram os dados e contribuíram para a redação e revisão do manuscrito.

MG, JAA e JCP: Contribuíram para a interpretação dos dados, a redação do manuscrito e a revisão crítica.

Todos os autores aprovaram a versão final a publicar.

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