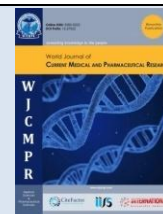




World Journal of Current Medical and Pharmaceutical Research

Content available at www.saap.org.in

ISSN: 2582-0222



HYPERREFLECTIVE FOCI AND DISORGANIZATION OF RETINAL INNER LAYERS AS PREDICTORS OF VISUAL PROGNOSIS IN DIABETIC MACULAR EDEMA

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DOI: <https://doi.org/10.37022/wjcmpr.v8i3.436>

ARTICLE HISTORY	ABSTRACT
Received on: 24-07-2026 Revised on: 16-08-2026 Accepted on: 02-10-2026	Background: Diabetic macular edema (DME) is a major cause of visual impairment, and optical coherence tomography biomarkers may help predict treatment outcomes. This study evaluated hyperreflective foci (HRF) and disorganization of retinal inner layers (DRIL) as predictors of visual prognosis in DME.
Keywords: Diabetic macular edema; DRIL; Hyperreflective foci; Optical coherence tomography; Visual prognosis	Methods: This prospective observational study included 80 eyes with DME treated with intravitreal anti-VEGF therapy and followed for 6 months. Best-corrected visual acuity (BCVA), central macular thickness (CMT), HRF count, DRIL extent, and other OCT biomarkers were assessed. Multivariable regression and ROC analyses were performed.
Corresponding Author Dr. Hannah Shiny R	Results: Mean BCVA improved from 0.60 to 0.48 logMAR, while CMT decreased from 470.9 to 357.8 μ m. DRIL extent showed a stronger correlation with 6-month BCVA than HRF count ($r=0.699$ vs 0.531). On multivariable analysis, DRIL extent, baseline BCVA, and ellipsoid-zone disruption independently predicted 6-month BCVA, whereas HRF count did not. DRIL showed an AUC of 0.829 for poor visual outcome.
	Conclusion: DRIL appears to be a stronger prognostic OCT biomarker than HRF in DME.

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INTRODUCTION

Diabetic macular edema (DME) is a leading cause of vision loss in patients with diabetic retinopathy and is caused primarily by breakdown of the blood-retinal barrier and subsequent retinal thickening and intraretinal fluid accumulation. In a pooled analysis of 35 population-based studies, the prevalence of DME was estimated to be around 6.8% of people with diabetes, and the burden of the disease was found to be higher with longer duration of diabetes, worse glycemic control and higher blood pressure [1]. Anti-vascular endothelial growth factor (anti-VEGF) drugs are the primary treatment for center-involving DME and can yield significant anatomic and functional benefit. But there is wide variability in treatment response among patients [2]. While CMT is a parameter routinely monitored, it only moderately correlates with visual acuity, and eyes with similar CMT can have very different visual outcomes [3]. As a result, there has been increased interest in the use of optical coherence tomography (OCT) biomarkers that more directly reflect retinal microstructural integrity. Hyperreflective foci (HRF) are small, discrete hyperreflective lesions seen on OCT and are believed to represent lipid extravasation, inflammatory

activity, activated microglia, or other retinal cellular changes. Bolz et al. showed an association between HRF and lipid extravasation in DME [4], and Uji et al. showed that outer retinal HRF were correlated with disruption of the photoreceptors and worse visual acuity [5]. HRF have also been explored as markers of treatment response, and decreases in HRF burden have been observed after anti-VEGF therapy [6].

Another significant OCT biomarker is disorganization of the retinal inner layers (DRIL). It is a sign of loss of identifiable boundaries between the inner retinal layers and is regarded as a marker of neural retinal injury. Sun et al. showed that both baseline DRIL and longitudinal changes in DRIL were associated with visual acuity in center-involving DME [7]. The association continued even after macular edema was resolved, indicating that DRIL may represent structural damage beyond retinal thickening [8].

HRF and DRIL could represent separate inflammatory and neurostructural aspects of DME, and assessing both together could enhance the prediction of functional outcome. The current study was thus designed to evaluate the predictive value of HRF and DRIL for visual prognosis in

patients with DME, especially in relation to visual acuity after 6 months of anti-VEGF therapy.

METHODS

Study design and participants

The study was a prospective observational study carried out at Sree Mookambika Institute of Medical Sciences, Kulasekharam, from March 2024 to March 2026. Eighty patients with diabetic macular edema (DME) were included, with one study eye per patient.

Demographic and systemic baseline variables were age, sex, residence, diabetes type and duration, HbA1c, insulin use, hypertension, dyslipidemia, and diabetic nephropathy. Ocular features were lens status, severity of DR, prior PRP, previous intravitreal treatment, and DME duration.

Visual acuity and OCT assessment

Best-corrected visual acuity (BCVA) was measured at baseline and at 1, 3 and 6 months and expressed in logMAR units for analysis. Central macular thickness (CMT) was measured and retinal biomarkers assessed using spectral-domain optical coherence tomography (SD-OCT).

Hyperreflective foci (HRF) were counted and classified as low (0–10), moderate (11–20) or high (>20). The presence or absence of disorganization of the retinal inner layers (DRIL) was noted and the extent of disorganization was measured in micrometers (μm); DRIL was classified as absent (0 μm), mild (1–250 μm), moderate (251–500 μm), or severe (>500 μm). Other OCT parameters were intraretinal cysts, subretinal fluid, hyperreflective subfoveal material, ellipsoid-zone disruption, external limiting membrane disruption, vitreomacular interface abnormality, and DME morphology.

Intravitreal anti-VEGF therapy with ranibizumab (0.5 mg/0.05 mL) was administered as clinically indicated, and patients were followed up for 6 months. The number of injections and use of rescue laser were recorded. CMT was reassessed at 1, 3 and 6 months, and HRF count and DRIL extent were reassessed at 6 months.

Outcome measures

The main outcome was 6-month BCVA (logMAR). The change in BCVA was obtained by subtracting the 6-month BCVA from the baseline BCVA; positive values represent improvement. A clinically meaningful visual improvement was considered to be ≥ 0.2 logMAR. Poor visual outcome was considered to be 6-month BCVA ≥ 0.5 logMAR. Anatomical response was determined by the change in CMT from baseline to follow-up.

Statistical analysis

Continuous variables were summarized as mean $\pm$ SD or median (IQR), and categorical variables as n (%). Paired t-tests assessed changes in BCVA and CMT over follow-up. Associations of HRF count and DRIL extent with 6-month BCVA and BCVA change were examined using Pearson correlation and linear regression. Group differences in BCVA were assessed by one-way ANOVA, categorical visual improvement by chi-square test, and BCVA between eyes with and without DRIL by independent-samples t-test with Welch correction when required.

Univariable and multivariable linear regression identified predictors of 6-month BCVA, including DRIL extent, HRF count, baseline BCVA and CMT, age, diabetes duration, HbA1c, DR severity, ellipsoid-zone disruption, subretinal fluid, and anti-VEGF injection number. Results were reported as β coefficients with 95% CIs, with R^2 , adjusted

R^2 , and variance inflation factors used to assess model performance and multicollinearity. Logistic regression assessed predictors of poor visual outcome, while ROC analysis evaluated DRIL, HRF, and their combined discriminatory ability. All tests were two-sided, with $p < 0.05$ considered statistically significant.

RESULTS

Participant characteristics

A total of 80 participants contributed one study eye each. The mean age was 58.0 ± 7.9 years; 50 (62.5%) were male and 75 (93.8%) had type 2 diabetes. The mean duration of diabetes was 12.4 ± 5.6 years and mean HbA1c was $8.5 \pm 1.1\%$. Moderate NPDR was the most frequent retinopathy grade, present in 36 (45.0%) eyes. Baseline demographic and clinical characteristics are summarized in Table 01.

Table 01: Baseline demographic and clinical characteristics (N=80)

Characteristic	Category/statistic	Value
Age, years	Mean $\pm$ SD	58.0 ± 7.9
	Median (IQR)	57.5 (53.0–63.0)
Sex	Male	50 (62.5%)
	Female	30 (37.5%)
Diabetes type	Type 1	5 (6.2%)
	Type 2	75 (93.8%)
Diabetes duration, years	Mean $\pm$ SD	12.4 ± 5.6
	Median (IQR)	12.5 (8.8–16.0)
HbA1c, %	Mean $\pm$ SD	8.5 ± 1.1
	Median (IQR)	8.5 (7.8–9.1)
Glycemic control	Good	6 (7.5%)
	Moderate	49 (61.2%)
	Poor	25 (31.2%)
Insulin use	—	28 (35.0%)
Hypertension	—	36 (45.0%)
Dyslipidemia	—	42 (52.5%)
Diabetic nephropathy	—	12 (15.0%)
Study eye	Right	42 (52.5%)
	Left	38 (47.5%)
Lens status	Phakic	65 (81.2%)
	Pseudophakic	15 (18.8%)
Diabetic retinopathy severity	Mild NPDR	12 (15.0%)
	Moderate NPDR	36 (45.0%)
	Severe NPDR	19 (23.8%)
	PDR	13 (16.2%)
Previous panretinal photocoagulation	—	13 (16.2%)
Previous intravitreal treatment	—	19 (23.8%)
DME duration, months	Mean $\pm$ SD	15.3 ± 6.5
	Median (IQR)	14.5 (10.0–19.2)

Baseline OCT and visual characteristics

Mean baseline BCVA was 0.60 ± 0.22 logMAR and mean CMT was 470.9 ± 67.1 μ m. DRIL was present in 36 (45.0%) eyes, high HRF burden in 23 (28.8%), and ellipsoid-zone disruption in 25 (31.2%). The baseline OCT profile is presented in Table 02.

Table 02: Baseline OCT and visual characteristics (N=80)

OCT characteristic	Category/statistic	Value
Baseline BCVA, log MAR	Mean $\pm$ SD	0.60 ± 0.22
	Median (IQR)	0.58 (0.44–0.75)
Baseline CMT, μ m	Mean $\pm$ SD	470.9 ± 67.1
	Median (IQR)	468.5 (425.5–510.5)
HRF count	Mean $\pm$ SD	17.4 ± 6.7
	Median (IQR)	17.0 (12.8–22.0)
HRF category	Low	14 (17.5%)
	Moderate	43 (53.8%)
	High	23 (28.8%)
DRIL present	Yes	36 (45.0%)
	No	44 (55.0%)
DRIL extent among DRIL-positive eyes, μ m	Mean $\pm$ SD	324.6 ± 175.4
	Median (IQR)	316.5 (212.8–432.5)
DRIL category	Absent	44 (55.0%)
	Mild	11 (13.8%)
	Moderate	21 (26.2%)
	Severe	4 (5.0%)
Intraretinal cysts	Yes	60 (75.0%)
	No	20 (25.0%)
Subretinal fluid	Yes	31 (38.8%)
	No	49 (61.2%)
Hyperreflective subfoveal material	Yes	20 (25.0%)
	No	60 (75.0%)
Ellipsoid-zone disruption	Yes	25 (31.2%)
	No	55 (68.8%)

External limiting membrane disruption	Yes	21 (26.2%)
	No	59 (73.8%)
Vitreomacular interface abnormality	Yes	13 (16.2%)
	No	67 (83.8%)
DME morphology	Diffuse retinal thickening	21 (26.2%)
	Cystoid macular edema	35 (43.8%)
	Serous retinal detachment	4 (5.0%)
	Mixed pattern	20 (25.0%)

Change in visual acuity and central macular thickness

Mean BCVA improved from 0.60 ± 0.22 logMAR at baseline to 0.48 ± 0.25 logMAR at 6 months, corresponding to a mean improvement of 0.124 logMAR (95% CI 0.093 to 0.155; paired $t=7.97$, $p<0.001$). Mean CMT decreased from 470.9 ± 67.1 μ m to 357.8 ± 55.0 μ m at 6 months (mean reduction 113.2 μ m; 95% CI 102.5 to 123.8; paired $t=21.08$, $p<0.001$). Changes at each follow-up are detailed in Table 03 and the BCVA trajectory is shown in Figure 01.

Table 03: Change in BCVA and central macular thickness during follow-up (N=80)

Outcome	Time point	Mean $\pm$ SD	Mean change	95 % CI	Paired t	p-value
BCVA (logMAR)	Baseline	0.60 ± 0.22	—	—	—	—
	1 month	0.56 ± 0.22	0.047	0.031 to 0.063	5.87	<0.001
	3 months	0.52 ± 0.24	0.084	0.059 to 0.108	6.76	<0.001
	6 months	0.48 ± 0.25	0.124	0.093 to 0.155	7.97	<0.001
CMT (μ m)	Baseline	470.9 ± 67.1	—	—	—	—
	1 month	408.4 ± 57.0	62.5	56.6 to 68.5	20.98	<0.001
	3 months	378.2 ± 53.8	92.7	84.4 to 101.1	22.06	<0.001
	6 months	357.8 ± 55.0	113.2	102.5 to 123.8	21.08	<0.001

Positive change denotes improvement in BCVA (baseline minus follow-up) and reduction in CMT (baseline minus follow-up).

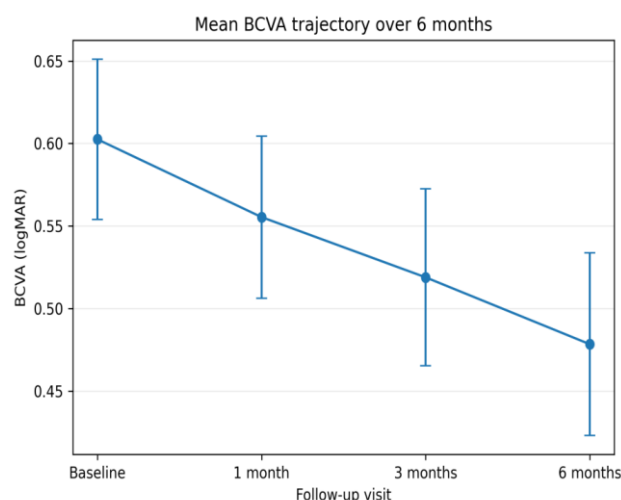


Figure 01: Mean BCVA trajectory from baseline to 6 months. Points indicate mean logMAR BCVA and error bars indicate 95% confidence intervals (N=80 at each visit). Lower logMAR values indicate better visual acuity.

Association of hyperreflective foci with visual outcome

Higher baseline HRF count was associated with worse 6-month BCVA, whereas HRF count was not associated with the magnitude of BCVA improvement. Six-month BCVA differed across HRF categories, but the proportion achieving a ≥ 2 -line improvement did not differ significantly between categories (Table 04).

Table 04: Association of baseline HRF with visual outcome

Exposure	Outcome	Analysis	Estimate	Additional information	Test statistic	p-value
HRF count (continuous)	6-month BCVA (logMAR)	Pearson correlation	$r = 0.531$	—	0.531	<0.001
HRF count (continuous)	6-month BCVA improvement	Pearson correlation	$r = -0.039$	—	-0.039	0.733
HRF count (per 10 foci)	6-month BCVA (logMAR)	Univariable linear regression	$\beta = 0.197$	0.126 to 0.268	$t = 5.54$	<0.001
HRF category: Low	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.29 ± 0.19	2 (14.3%)	—	—
HRF category: Moderate	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.44 ± 0.21	15 (34.9%)	—	—
HRF category: High	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.66 ± 0.24	6 (26.1%)	—	—
HRF category	6-month BCVA (logMAR)	One-way ANOVA	—	$df = 2, 77$	$F = 14.82$	<0.001
HRF category	≥ 2 -line visual improvement	Pearson chi-square	—	$df = 2$	$\chi^2 = 2.30$	0.317

Association of DRIL with visual outcome

Eyes with baseline DRIL had worse 6-month BCVA than eyes without DRIL. Greater DRIL extent showed a strong positive correlation with 6-month logMAR BCVA, while its association with the magnitude of visual improvement did not reach statistical significance. Six-month BCVA also worsened progressively across DRIL severity categories (Table 05).

Table 05: Association of baseline DRIL with visual outcome

Exposure	Outcome	Analysis/group	Estimate	Additional information	Test statistic	p-value
DRIL presence: Yes	6-month BCVA (logMAR)	Mean $\pm$ SD	0.63 ± 0.24	$n = 36$	—	—
DRIL presence: No	6-month BCVA (logMAR)	Mean $\pm$ SD	0.35 ± 0.18	$n = 44$	—	—
DRIL presence	6-month BCVA (logMAR)	Welch t-test	—	$df = 62.5$	$t = 5.70$	<0.001
DRIL extent (continuous)	6-month BCVA (logMAR)	Pearson correlation	$r = 0.699$	—	0.699	<0.001

DRIL extent (continuous)	6-month BCVA improvement	Pearson correlation	$r = -0.196$	—	-0.196	0.081
DRIL category: Absent	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.35 ± 0.18	15 (34.1%)	—	—
DRIL category: Mild	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.46 ± 0.23	3 (27.3%)	—	—
DRIL category: Moderate	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.67 ± 0.20	5 (23.8%)	—	—
DRIL category: Severe	6-month BCVA / ≥ 2 -line improvement	Descriptive	0.90 ± 0.18	0 (0.0%)	—	—
DRIL category	6-month BCVA (logMAR)	One-way ANOVA	—	df = 3,76	F = 19.60	<0.001
DRIL category	≥ 2 -line visual improvement	Pearson chi-square	—	df = 3	$\chi^2 = 2.49$	0.477

Predictors of 6-month visual acuity

In univariable linear regression, greater DRIL extent, higher HRF count, worse baseline BCVA, greater baseline CMT, longer diabetes duration, higher HbA1c, more severe diabetic retinopathy, ellipsoid-zone disruption, and a higher injection count were associated with worse 6-month BCVA. Age and subretinal fluid were not significantly associated with 6-month BCVA (Table 06).

Table 06: Univariable predictors of 6-month BCVA (logMAR)

Predictor	β	SE	95% CI	t statistic	p-value	R ²
Baseline DRIL extent (per 100 μm)	0.087	0.010	0.067 to 0.107	8.64	<0.001	0.489
Baseline HRF count (per 10 foci)	0.197	0.036	0.126 to 0.268	5.54	<0.001	0.282
Baseline BCVA (per 0.1 logMAR)	0.095	0.007	0.080 to 0.109	13.16	<0.001	0.689
Baseline CMT (per 100 μm)	0.083	0.041	0.002 to 0.165	2.03	0.046	0.050
Age (per 10 years)	0.020	0.036	-0.050 to 0.091	0.57	0.567	0.004
Diabetes duration (per 5 years)	0.087	0.023	0.041 to 0.133	3.76	<0.001	0.154
HbA1c (per 1%)	0.069	0.025	0.019 to 0.118	2.77	0.007	0.090
DR severity (per category)	0.123	0.027	0.070 to 0.176	4.60	<0.001	0.213
Ellipsoid-zone disruption	0.325	0.048	0.229 to 0.420	6.77	<0.001	0.370
Subretinal fluid	0.031	0.057	-0.083 to 0.145	0.54	0.589	0.004
Anti-VEGF injections (per injection)	0.060	0.027	0.007 to 0.113	2.25	0.027	0.061

The multivariable linear regression model explained 75.9% of the variance in 6-month BCVA ($R^2=0.759$; adjusted $R^2=0.720$; $F(11, 68)=19.47$, $p<0.001$). Greater DRIL extent, worse baseline BCVA, and ellipsoid-zone disruption remained independently associated with worse 6-month BCVA. HRF count did not remain independently associated after adjustment (Table 07 and Figure 02).

Table 07: Multivariable predictors of 6-month BCVA (logMAR)

Predictor	β	SE	95% CI	t statistic	p-value	VIF
Baseline DRIL extent (per 100 μm)	0.039	0.011	0.016 to 0.061	3.45	<0.001	2.29
Baseline HRF count (per 10 foci)	0.027	0.032	-0.037 to 0.092	0.84	0.403	2.16
Baseline BCVA (per 0.1 logMAR)	0.060	0.014	0.032 to 0.087	4.30	<0.001	4.20
Baseline CMT (per 100 μm)	-0.007	0.031	-0.068 to 0.053	-0.24	0.807	1.91
Age (per 10 years)	0.007	0.020	-0.033 to 0.047	0.34	0.737	1.15
Diabetes duration (per 5 years)	-0.023	0.018	-0.059 to 0.014	-1.23	0.221	1.91
HbA1c (per 1%)	0.003	0.017	-0.031 to 0.038	0.19	0.848	1.58
DR severity (per category)	-0.000	0.024	-0.049 to 0.049	-0.00	0.998	2.38
Ellipsoid-zone disruption	0.096	0.044	0.008 to 0.184	2.17	0.034	1.93
Subretinal fluid	-0.033	0.036	-0.105 to 0.040	-0.90	0.370	1.43
Anti-VEGF injections (per injection)	0.001	0.019	-0.037 to 0.038	0.04	0.965	1.69

Model: $R^2=0.759$; adjusted $R^2=0.720$; $F(11,68)=19.47$, $p<0.001$. Maximum VIF=4.20.

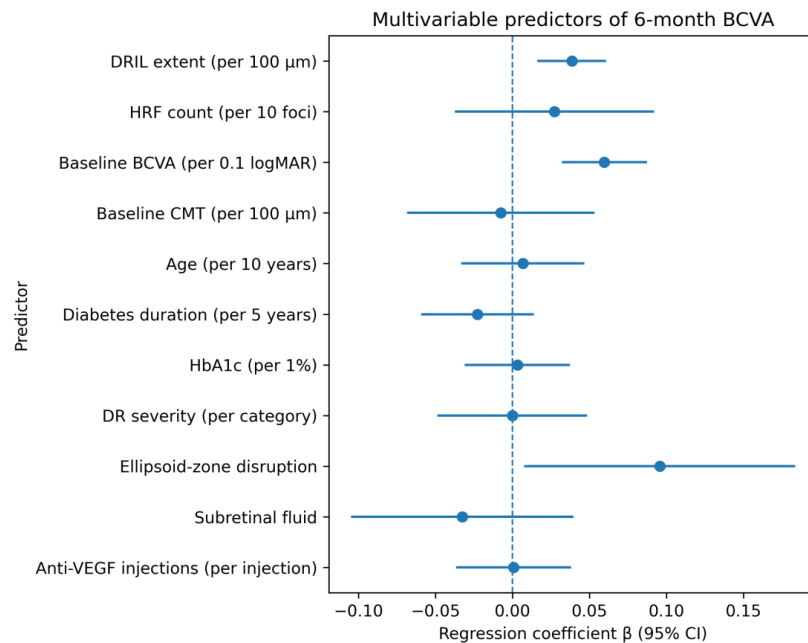


Figure 02: Multivariable predictors of 6-month BCVA. Points represent adjusted regression coefficients (β) and horizontal lines represent 95% confidence intervals (N=80). Positive coefficients indicate worse 6-month logMAR BCVA.

Secondary prediction analyses

Poor visual outcome, defined as 6-month BCVA ≥ 0.5 logMAR, occurred in 35 (43.8%) eyes. In the adjusted logistic model, DRIL extent per 100 μm remained associated with poor visual outcome (adjusted OR 2.10, 95% CI 1.13 to 3.88; Wald $\chi^2=5.53$, $p=0.019$), whereas HRF count per 10 foci did not (adjusted OR 0.61, 95% CI 0.10 to 3.87; Wald $\chi^2=0.27$, $p=0.602$). On exploratory ROC analysis, the AUC was 0.829 (95% CI 0.731 to 0.914) for DRIL extent, 0.740 (95% CI 0.619 to 0.843) for HRF count, and 0.886 (95% CI 0.803 to 0.950) for the combined DRIL-plus-HRF model.

DISCUSSION

In this prospective study of 80 eyes with DME, anti-VEGF therapy was followed by significant anatomical and functional improvement after 6 months. The mean BCVA improved from 0.60 to 0.48 logMAR, and the mean central macular thickness (CMT) was reduced from 470.9 to 357.8 μm . Baseline HRF count was correlated with 6-month BCVA ($r=0.531$), while disorganization of the retinal inner layers (DRIL) was more strongly correlated ($r=0.699$). HRF count and CMT were not independently associated with final vision after multivariable adjustment, but DRIL extent, baseline BCVA, and ellipsoid-zone disruption were. The results indicate that retinal microstructural integrity may offer more prognostic value than retinal thickness.

The prognostic value of DRIL in our study is in line with previous studies. Radwan et al. found that eyes with DRIL had poorer visual acuity at baseline and after resolution of center-involved DME, and that longer total DRIL was associated with poorer subsequent vision after adjusting for baseline acuity [9]. Das et al. also reported that increasing DRIL was correlated with poorer visual acuity and that DRIL was more common in eyes with external limiting membrane disruption, ellipsoid-zone disruption and proliferative diabetic retinopathy [10]. These observations are consistent with our observation that both DRIL extent and ellipsoid-zone disruption independently predicted 6-

month BCVA, indicating that DRIL may be a marker of more advanced neural and photoreceptor injury rather than just a marker of edema severity.

Evidence from steroid-treated DME also supports DRIL as a functionally meaningful biomarker. Zur et al. showed that eyes without baseline DRIL had better visual and anatomical responses, and that there was partial improvement of DRIL during dexamethasone treatment [11]. Our patients were treated with anti-VEGF, but the same principle could apply: even with ongoing neural disorganization, anatomical drying may occur, and this could restrict visual recovery. This may account for the significant drop in CMT but the lack of independent prognostic value after adjustment.

The predictive behaviour of HRF was more complex. HRF burden was correlated with worse final BCVA in univariable analysis, but was not correlated with the amount of visual improvement and was not significant in multivariable analysis. Vujosevic et al. found a significant decrease in HRF after anti-VEGF treatment together with improvement in vision, but HRF number itself was not significantly associated with BCVA [12]. Likewise, Arthi et al. found HRF to be associated with structural features of DME, such as cystoid spaces and subretinal fluid, indicating that HRF may represent an exudative or inflammatory phenotype rather than fixed neural damage [13].

The prognostic significance of HRF may also be related to their retinal location. Huang et al. demonstrated that outer-retinal HRF correlated with greater visual and anatomical improvement following anti-VEGF treatment, while inner-retinal HRF correlated with worse baseline visual acuity [14]. Conversely, Tang et al. reported that outer-retinal HRF correlated with poorer ELM and EZ integrity, with better final visual acuity in eyes with preserved outer-retinal structures [15]. The seemingly conflicting results indicate that HRF could be a marker of disease activity and/or treatment responsiveness depending on their location and associated retinal damage. Because HRF were evaluated mainly by total count in our study, layer-specific associations may have been diluted.

One important finding was that CMT was not an independent predictor. While the mean CMT reduced by over 100 μm , baseline CMT was not independently associated with final BCVA. This is consistent with the notion that retinal thickness is largely a measure of fluid accumulation, while DRIL and ellipsoid-zone disruption are more direct measures of tissue integrity. Similarly, diabetes duration, HbA1c, retinopathy severity and number of injections were no longer significant after multivariable adjustment, possibly because some of these effects may be mediated by retinal structural damage.

The secondary analyses also support the potential of OCT biomarkers for risk stratification. Poor visual outcome occurred in 43.8% of eyes, with DRIL extent remaining independently associated with poor visual outcome, whereas HRF count did not. The ROC AUC was 0.829 for DRIL, 0.740 for HRF, and 0.886 for the combined model. These results suggest that the combined model may provide additional prognostic information but should be used with caution as it was derived and tested in the same relatively small cohort.

STRENGTHS AND LIMITATIONS

The study has several strengths, such as prospective follow-up, standardized serial OCT and BCVA assessment, and direct multivariable comparison of DRIL and HRF. The small sample size, 6-month follow-up, non-randomized treatment, some eyes treated with intravitreal therapy prior to enrollment, absence of layer-specific HRF analysis, and absence of direct macular ischemia assessment are limitations. There is a need for larger, externally validated studies with standardized treatment and more detailed OCT characterization.

CONCLUSION

DRIL showed stronger prognostic value than HRF in diabetic macular edema treated with anti-VEGF therapy. Baseline DRIL extent, baseline BCVA, and ellipsoid-zone disruption were independent predictors of 6-month vision, while HRF burden and central macular thickness were not. The results of this study suggest that DRIL is a potentially useful OCT biomarker for visual prognosis in DME, but further studies with larger numbers of patients and longer follow-up are required to validate these findings.

FUNDING

Nil

CONFLICT OF INTEREST

Not Declared

ACKNOWLEDGEMENT

Not Declared

AUTHOR CONTRIBUTION

All authors are contributed equally

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