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The diagnostic value of platelet-to-neutrophil ratio in diabetic macular edema

Huixin Sun[1], Yao Li[1], Shihan Liu[1], Chunxing Pan[1], Danting Li[1] and Xiyuan Zhou[1*]

Abstract

Purpose To evaluate the diagnostic value of platelet-to-neutrophil ratio (PNR) in the occurrence of diabetic macular edema (DME) in patients with diabetic retinopathy (DR).

Methods This cross-sectional study included 366 participants categorized into four groups: DME group ($n=96$), DR group ($n=90$, DR without DME), diabetes mellitus (DM) group ($n=90$, without DR), and healthy control group ($n=90$). PNR was calculated by dividing the platelet count by the neutrophil count. Each subject was classified as one of three DME types according to the optical coherence tomography (OCT) features: diffuse retinal thickening (DRT), cystoid macular edema (CME), serous retinal detachment (SRD). The correlations between the PNR and the occurrence of DME, as well as the DME subtypes based on OCT were investigated. Multivariate logistic regression analysis was employed to determine the risk factors for DME. Receiver operating characteristic (ROC) curve analysis was conducted to assess the predictive value of PNR for DME.

Results DME group exhibited significantly lower PNR level compared to the other three groups [50.73 (38.92, 65.20) in DME group, 95.63 (68.83, 120.19) in DR group, 92.39 (72.38, 130.61) in DM group, and 100.66 (75.26, 152.77) in healthy control group, respectively, $p<0.001$], but did not differ across the DME subtypes based on OCT ($p=0.548$). The ROC curve demonstrated that the PNR could better predict DME (area under the curve = 0.832, 95% confidence interval: 0.773 - 0.891, $p<0.001$). When the cut-off value of the PNR was 68.51, the sensitivity was 80.2%, and the specificity was 75.6%. Multivariate regression analysis indicated that PNR ≤ 68.51 was an independent risk factor for DME occurrence in DR patients (Odds ratio = 12.05, 95% confidence interval: 5.93 - 24.47, $p<0.001$).

Conclusion PNR ≤ 68.51 was strongly associated with the development of DME in DR patients, while no significant differences in PNR levels were observed across the different OCT morphological groups. Hence, PNR may serve as a valuable diagnostic biomarker for identifying DME, thereby enhancing risk stratification and management strategies for patients with DR.

Keywords Diabetic macular edema, Diabetic retinopathy, Platelet-to-neutrophil ratio, Optical coherence tomography, Diagnostic value

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Introduction

Diabetes mellitus (DM) is a prevalent chronic metabolic disorder that poses a significant threat to human health. Diabetic retinopathy (DR), one of the most frequent microvascular complications associated with DM, can lead to severe visual impairment. Additionally, diabetic macular edema (DME), in particular, is a predominant cause of disabling central vision loss in individuals with DR, and it may manifest at any stage of the disease, affecting approximately 7% of people with DM [1]. The pathogenesis of DME is multifaceted, with the primary mechanism underlying the development and progression of macular edema being the upregulated secretion of pro-angiogenic and pro-inflammatory factors [2]. This dysregulation culminates in dysfunctional vascular endothelial cells and pericytes, which are critical to maintaining the integrity of the retinal microvasculature [2].

Recently, there has been a growing clinical focus on the use of absolute blood cell counts and their ratios as inflammatory markers in DR and DME [3, 4, 5]. Platelet-to-neutrophil ratio (PNR) stands out as a novel biomarker, integrating platelet and neutrophil counts to provide a comprehensive assessment of the extent of clot formation and inflammation, as well as their interplay. While numerous studies have explored the utility of this index in the field of cerebrovascular diseases, with some indicating that a lower PNR was associated with worse outcomes [6, 7], few studies investigated the relationship between PNR and DR or DME. Building on this foundation, we sought to elucidate the association between PNR with DME, and to assess PNR and other peripheral blood inflammatory indices whether could be accepted as biomarkers of DME.

Material and method

This retrospective and cross-sectional study was carried out in the Department of Ophthalmology at the Second Affiliated Hospital of Chongqing Medical University between September 2020 and October 2023.

Ethical approval

The study protocol and procedures received ethical approval from the Institutional Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University [approval number: 2024(26)] and were conducted in compliance with the tenets of the Declaration of Helsinki. The requirement for informed consent was waived because this study was based on routinely collected claims data. Demographic details, results of ophthalmic examinations, and laboratory test results were meticulously reviewed from the patients' medical files and hospital records.

Study participants

This study enrolled patients with type 2 DM aged ≥ 18 years who had been previously diagnosed and had complete medical records; these patients were further categorized into the DME group, DR group, and DM group. DR and DME were diagnosed through clinical examination and further confirmed by optical coherence tomography (OCT) as well as fundus fluorescein angiography (FFA). The DME group was subsequently subdivided into three categories based on the different morphological patterns observed on OCT: cystoid macular edema (CME) group, diffuse retinal thickening (DRT) group, and severe retinal detachment (SRD) group [8] (Fig. 1). Healthy controls comprised cataract surgery patients aged ≥ 18 years without underlying systemic medical conditions or other ocular pathologies, who also had complete medical records.

Patients were excluded from the study if they met any of the following criteria: (1) a history of ocular interventions such as intravitreal injections or vitreoretinal surgery; (2) presence of other concurrent ocular pathologies including but not limited to posterior uveitis, glaucoma, retinal vascular occlusion, or age-related macular degeneration; (3) a recent history of acute coronary events or stroke within the past 3 months; (4) a history of acute or chronic systemic infectious diseases, anemia, cancer, acute coronary syndrome, cerebrovascular disease, trauma, hepatic or renal insufficiency; (5) current use

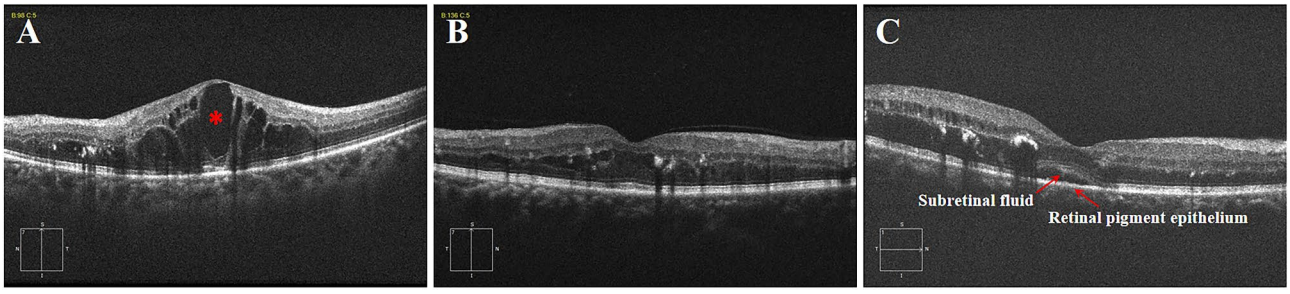

Fig. 1 Performance of different morphological patterns of DME based on OCT. (**A**) Cystoid macular edema (CME) edemas are clinically defined as a hyporeflective cystoid space (Red asterisks) surrounded by highly reflective membranes that represent the "cystoid-cavities"; (**B**) Diffuse retinal thickening (DRT) edemas typically proliferate in the outer retina layer with a "sponge-like" appearance; (**C**) Severe retinal detachment (SRD) edemas show subretinal fluid between retinal nerve epithelium and pigment epithelium

of systemic or topical non-steroidal anti-inflammatory drugs, antibiotics, immunosuppressants, anticoagulants, antiplatelet agents, steroid, or oral contraceptives; (6) a history of ocular surgery within the previous 6 months; (7) absence or poor quality of OCT images.

Clinical examination and biochemical analysis

All participants underwent a comprehensive routine medical examination and a detailed ophthalmic assessment including slit-lamp biomicroscopy, best-corrected visual acuity (BCVA), color fundus photography, intraocular pressure (noncontact tonometer), and OCT. Their medical history and records were meticulously reviewed, and DR was classified according to the International Clinical Diabetic Retinopathy Disease Severity Scale [9]. The evaluation of DR was conducted by ophthalmologists who were blinded to our study's objectives. OCT was performed to evaluate the different morphological patterns of DME using an OCT system (ZEISS CIRRUS HD-OCT 5000). All OCT scans were conducted by a seasoned physician who was blinded to the patients' visual acuity when interpreting the images.

After an overnight fast, venous blood samples of participants were collected from antecubital veins. Complete blood cell counts with differential counts were performed in our hospital. Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) were defined as the ratios of neutrophil to lymphocyte, monocyte to lymphocyte, and platelet to lymphocyte counts, respectively. Systemic immune-inflammation index (SII) value was calculated using the formula: platelet count × (neutrophil count / lymphocyte count) [10], while systemic inflammation response index (SIRI) value was derived as: neutrophil count × monocyte count / lymphocyte count [11]. Additionally, PNR was obtained by dividing platelet count by neutrophil count.

Statistical analysis

All statistical analyses were performed by SPSS software (version 26.0, IBM, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) for normally distributed data and median (interquartile range [IQR]) for non-normally distributed data. Numbers (percentages) were used to represent categorical variables. Depending on the distribution of the data, we used Kruskal-Wallis tests or one-way ANOVA for comparison. To find the significant differences between particular groups, post hoc analysis was performed using either Dunn's test or Bonferonni's correction. Categorical variables were analyzed using the χ^2 test. The optimal PNR cutoff values for predicting DME were found using receiver operating characteristic (ROC) curve analysis, with the prediction accuracy was quantified by the area under the ROC curve (AUC). PNR and the occurrence of DME were found to be associated by binary logistic regression analysis. $p < 0.05$ was determined to be the accepted significance level.

Result

The study population comprised 366 participants categorized into four groups: DME group ($n = 96$), DR group ($n = 90$, DR without DME), diabetes mellitus (DM) group ($n = 90$, without DR), and healthy control group ($n = 90$). The demographic and laboratory parameters of the study population were summarized in Table 1. No significant differences were observed among the groups with respect to sex, age, and history of hypertension ($p > 0.05$, for all). Post hoc analysis revealed that the duration of DM was comparable between the DME and DR groups ($p = 1.000$) and significantly longer than that in the DM group ($p < 0.001$, $p = 0.005$). In terms of DR disease severity scale, the proportion of proliferative diabetic retinopathy (PDR) in DME group was significantly higher compared to the DR group. The white blood cell count, monocyte count, platelet count, and PLR did not significantly differ across the four groups ($p > 0.05$, for all). However, neutrophil count, lymphocyte count, platelet distribution width (PDW), mean platelet volume (MPV), NLR, MLR, SII, and SIRI showed significant variations between groups. Post hoc analysis findings are summarized in Fig. 2. Neutrophil count was significantly higher in the DME group compared to the healthy control (HC) group ($p = 0.006$), it was similar among the other three groups ($p > 0.05$, for all, Fig. 2A). Lymphocyte count was significantly higher in the DM group compared to the DME group ($p = 0.014$, Fig. 2B), while the level of PDW was higher in the DM group compared to the HC group ($p = 0.030$, Fig. 2C). Additionally, post hoc analysis showed that MPV, NLR, MLR, and SIRI were significantly higher in the DME group compared to the DM and HC groups ($p < 0.05$, for all), but were comparable between the DME and DR groups ($p > 0.05$, for all, Fig. 2D - F, H). Furthermore, we found that the PNR was significantly lower in the DME group compared to the other three groups ($p < 0.05$, for all), while it remained similar among the remaining groups ($p > 0.05$, for all, Fig. 2I). However, SII values were consistent across the four groups (Fig. 2G).

The ROC curve was depicted in Fig. 3 to determine the best cutoff value of the PNR to predict DME. A PNR of 68.51 emerged as the best threshold for predicting DME, offering a sensitivity of 80.2% and a specificity of 75.6% [area under the curve (AUC): 0.832, 95% confidence interval (CI): 0.773–0.891, $p < 0.001$]. Binary logistic regression analysis showed that PNR ≤ 68.51 was significantly associated with DME prediction [odds ratio (OR): 12.05, 95% CI: 5.93–24.47, $p < 0.001$]. Besides, patients with PDR were found to be at a higher risk of developing

Table 1 Demographic and laboratory parameters of study population

Variable	DME ($n=96$)	DR ($n=90$)	DM ($n=90$)	HC ($n=90$)	*p* value
Gender, n (%)					0.489
Male	50 (52.1%)	44 (48.9%)	39 (43.3%)	38 (42.2%)	
Female	46 (47.9%)	46 (51.1%)	51 (56.7%)	52 (57.8%)	
Age (years)	61.00 ± 9.28	62.07 ± 9.26	63.01 ± 5.51	63.44 ± 6.95	0.158
Duration of diabetes (years)	11.50 (8.25, 20.00)	10.00 (6.00, 20.00)	10.00 (2.00, 10.00)	/	**< 0.001**
Hypertension, n (%)	44 (45.8%)	40 (44.4%)	40 (44.4%)	/	0.976
DR disease severity scale, n (%)					**0.011**
Mild-Moderate NPDR	38 (39.6%)	53 (58.9%)	/	/	
Severe NPDR	27 (28.1%)	23 (25.6%)	/	/	
PDR	31 (32.3%)	14 (15.5%)	/	/	
White blood cell count, (*10^9/L)	6.24 ± 1.46	6.11 ± 1.42	6.31 ± 1.48	5.82 ± 1.25	0.093
Neutrophil, (*10^9/L)	3.99 ± 1.22	3.79 ± 1.13	3.87 ± 1.33	3.43 ± 0.90[a]	**0.008**
Lymphocyte, (*10^9/L)	1.62 ± 0.49	1.73 ± 0.59	1.86 ± 0.53[a]	1.80 ± 0.57	**0.018**
Monocyte, (*10^9/L)	0.42 ± 0.15	0.41 ± 0.13	0.39 ± 0.11	0.39 ± 0.12	0.150
Platelet, (*10^9/L)	198.06 ± 56.55	204.27 ± 58.40	200.26 ± 43.00	204.99 ± 51.57	0.781
Platelet distribution width, (fL)	15.17 ± 2.60	15.37 ± 2.01	15.89 ± 1.72	14.91 ± 2.59[c]	**0.029**
Mean platelet volume, (fL)	11.49 ± 1.21	11.37 ± 1.36	10.87 ± 1.34[a]	10.41 ± 1.43[ab]	**< 0.001**
NLR	2.45 (1.79, 3.38)	2.06 (1.61, 2.96)	2.06 (1.49, 2.69)[a]	2.04 (1.49, 2.48)[a]	**0.002**
MLR	0.25 (0.20, 0.32)	0.23 (0.19, 0.32)	0.21 (0.15, 0.27)[a]	0.20 (0.17, 0.28)[a]	**< 0.001**
PLR	124.45 (91.49, 157.45)	125.49 (87.08, 157.00)	108.52 (85.88, 124.24)	120.09 (90.07, 136.07)	0.106
SII	465.62 (329.32, 638.81)	415.05 (284.45, 700.12)	382.63 (290.05, 546.67)	409.95 (312.50, 507.49)	**0.041**
SIRI	1.05 (0.62, 1.35)	0.83 (0.63, 1.16)	0.75 (0.52, 1.14)[a]	0.76 (0.51, 0.91)[a]	**< 0.001**
PNR	50.73 (38.92, 65.20)	95.63 (68.83, 120.19)[a]	92.39 (72.38, 130.61)[a]	100.66 (75.26, 152.77)[a]	**< 0.001**

DME: Diabetic macular edema; DR: Diabetic retinopathy; DM: Diabetes mellitus; HC: Healthy control; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; PNR: Platelet-to-neutrophil ratio

[a]Significant difference between the group and DME group; [b]Significant difference between the group and DR group; [c]Significant difference between the group and DM group

DME, with a sensitivity of 60.4% and a specificity of 58.9% (OR: 2.59, 95% CI: 1.06–6.33, $p=0.038$) (Table 2).

The DME group was stratified into three subgroups according to different morphological patterns based on OCT as CME group ($n=44$), DRT group ($n=21$), and SRD group ($n=31$). The demographic and laboratory parameters of these subgroups were summarized in Table 3. Significant differences were noted in age, duration of DM, lymphocyte count, MLR, and PLR across the groups. Post hoc analysis revealed that the age, the duration of DM, and lymphocyte count were significantly higher in the CME group compared to the SRD group ($p<0.05$, for all), while MLR was significantly lower ($p<0.05$, for all). Additionally, post hoc analysis showed that the duration of DM and PLR were significantly higher in the DRT group than in the SRD group ($p=0.006$ and $p=0.029$, respectively), with no significant differences observed between the CME and DRT groups. However, PNR remained comparable across all three groups.

Discussion

In this study, we demonstrated that DR patients with a lower PNR were more likely to develop DME. Furthermore, our further analyses revealed a threshold effect, which, to the best of our knowledge, was the first to be reported in the context of PNR as a novel inflammatory marker and its relationship with DME.

PNR is a groundbreaking biomarker that amalgamates platelet count and neutrophil count, providing a more holistic reflection of the intensity of thrombotic and inflammatory processes, as well as their interplay. However, PNR has been scarcely studied in the ophthalmic field. In the research on Graves' orbitopathy (GO), PNR is one of the important research indicators. The study of Abounoori et al. [12] found that the PNR levels in GO patients vary under different disease conditions. The PNR in active GO patients is significantly lower than that in non-active patients ($p<0.001$), and the PNR in moderate to severe GO patients is significantly lower than that in mild patients ($p=0.009$), suggesting its relation to GO activity and severity, with lower PNR linked to disease progression and increased severity.

In the field of cerebrovascular diseases, similar to the results of our study, the lower the PNR level, the more severe the disease results tends to be. PNR is a significant predictor in acute ischemic stroke. It can predict hemorrhagic transformation (HT), with low PNR patients having a higher HT risk (AUC = 0.808, 95% CI: 0.735 - 0.882, $p<0.05$) [13]. Post-intravenous thrombolysis PNR is

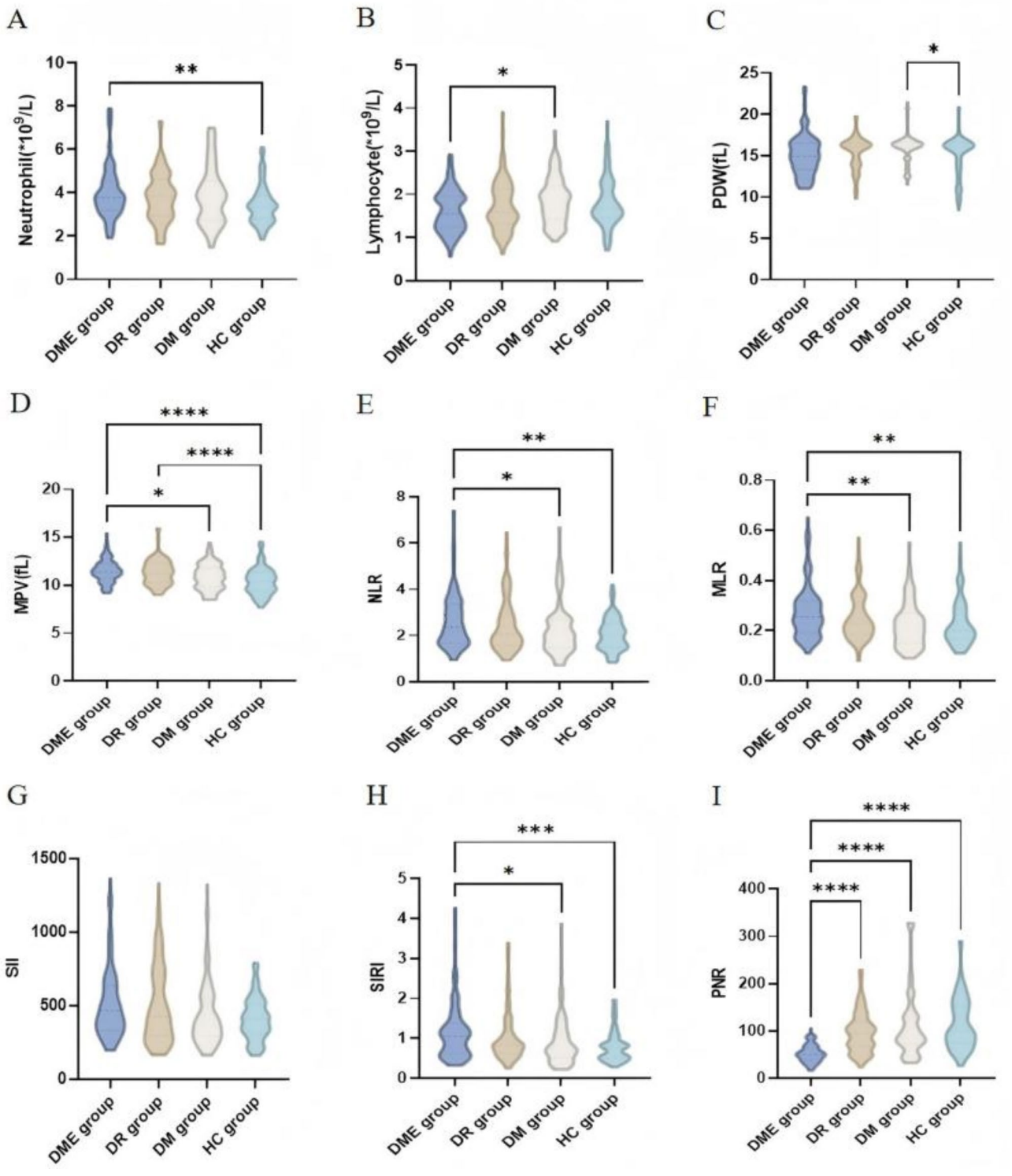

Fig. 2 Comparative analysis of peripheral blood laboratory indices among the 4 groups. (**A**) Neutrophil; (**B**) Lymphocyte; (**C**) Platelet distribution width (PDW); (**D**) Mean platelet volume (MPV); (**E**) Neutrophil-to-lymphocyte ratio (NLR); (**F**) Monocyte-to-lymphocyte ratio (MLR); (**G**) Systemic immune-inflammation index (SII); (**H**) Systemic inflammation response index (SIRI); (**I**) Platelet-to-neutrophil ratio (PNR). *$p < 0.05$, **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$

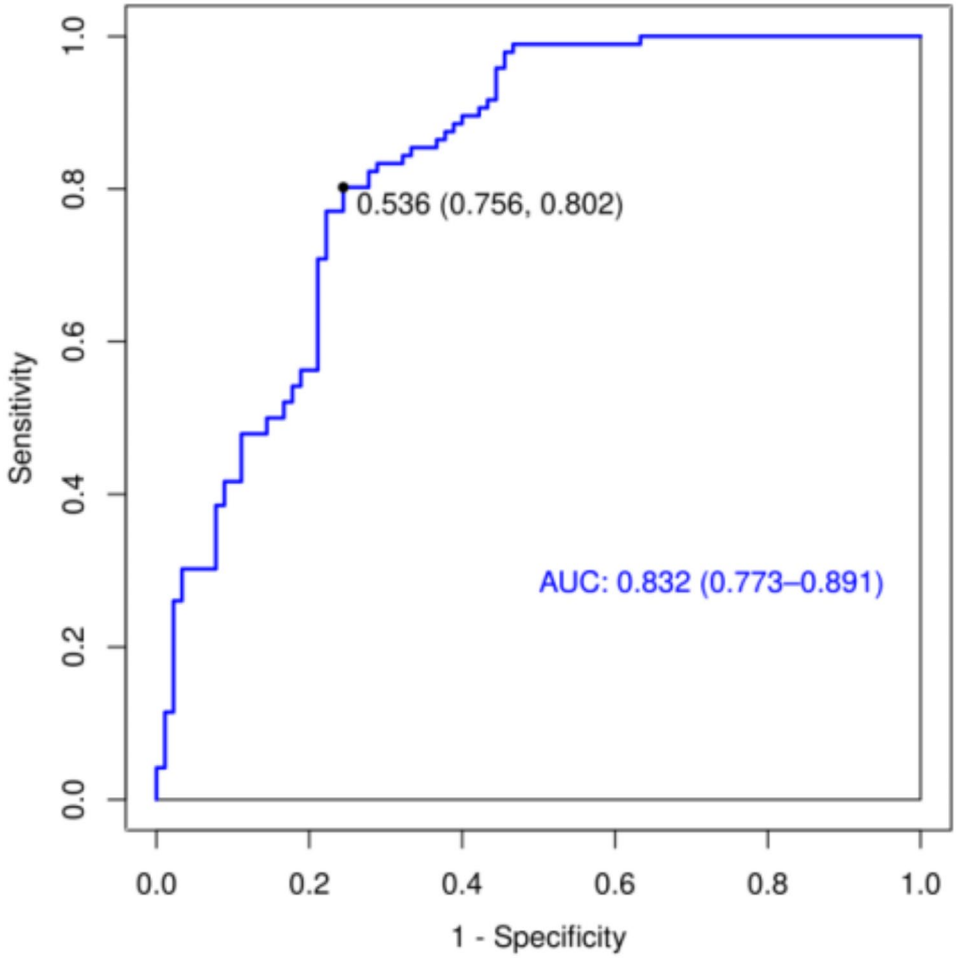

Fig. 3 ROC curve of PNR for predicting the occurrence of DME in patients with DR. Area under the curve (AUC) = 0.832, 95% confidence interval: 0.773 - 0.891, $p < 0.001$. When the cut-off value of the PNR was 68.51, the sensitivity was 80.2%, and the specificity was 75.6%

Table 2 Univariate and multivariate logistic regression analysis of the occurrence of DME in patients with DR

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*p* value	OR (95%CI)	*p* value
PNR ≤ 68.51	12.53 (6.25 - 25.10)	**<0.001**	12.05 (5.93 - 24.47)	**<0.001**
DR-Severe NPDR	1.64 (0.82 - 3.28)	0.164	1.22 (0.53 - 2.80)	0.642
DR-PDR	3.09 (1.45 - 6.58)	**0.003**	2.59 (1.06 - 6.33)	**0.038**

OR: Odds ratio; CI: Confidence interval; PNR: Platelet-to-neutrophil ratio; DR: Diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy

independently related to early and delayed neurological deterioration, HT, and a poor 3-month outcome, where lower PNR indicates a worse prognosis [7]. Also, a lower admission PNR is linked to a poor 90-day prognosis in AIS patients. Multivariate logistic regression shows PNR is an independent protective factor for predicting AIS prognosis, and it's more accurate than PLR and platelet-to-white blood cell ratio in predicting the 3-month prognosis of acute ischemic cerebral infarction [6].

Emerging studies have characterized platelet as a type of immune and inflammatory cell [14]. Platelets play a crucial role in the pathogenesis of both DR and DME. The enhanced activation and aggregation of platelets are significant contributors to vascular complications in diabetes [15], and significant reductions in platelet levels have been observed in DR patients compared to those without retinopathy [16]. There are multiple reasons for this. Firstly, we postulated that consumption during coagulation mainly attributes to decreased platelets in DR patients. The hypercoagulable state in diabetes, due to abnormal platelet function and the activation of the coagulation cascade, leads to increased platelet consumption during clot formation. Secondly, inflammatory cytokines and excessive reactive oxygen species can

Table 3 Demographic and laboratory parameters of study population between different morphological patterns based on OCT

Variable	CME (*n* = 44)	DRT (*n* = 21)	SRD (*n* = 31)	F/H/χ2	*p* value
Gender, n(%)				2.16	0.340
Male	26 (59.1%)	16 (76.2%)	18 (58.1%)		
Female	18 (40.9%)	5 (23.8%)	13 (41.9%)		
Age (years)	64.00 (57.25, 70.00)	64.00 (57.00, 67.00)	58.00 (50.00, 64.50)[a]	6.68	**0.035**
Duration of diabetes (years)	12.50 (9.75, 20.00)	16.00 (12.00, 20.00)	10.00 (3.50, 14.00)[ab]	10.57	**0.005**
Hypertension, n (%)	19 (43.2%)	10 (47.6%)	15 (48.4%)	0.23	0.890
DR disease severity scale, n (%)				1.97	0.742
Mild-Moderate NPDR	20 (45.4%)	6 (28.6%)	12 (38.7%)		
Severe NPDR	12 (27.3%)	7 (33.3%)	8 (25.8%)		
PDR	12 (27.3%)	8 (38.1%)	11 (35.5%)		
BCVA (logMAR)	0.60 (0.30, 0.82)	0.70 (0.33, 0.82)	0.70 (0.40, 0.92)	0.69	0.707
White blood cell count, (*10^9/L)	6.00 (5.36, 6.77)	5.96 (5.08, 6.34)	6.11 (5.66, 6.71)	1.00	0.606
Neutrophil, (*10^9/L)	3.77 (3.17, 4.56)	3.72 (3.43, 4.29)	3.87 (3.06, 4.48)	0.12	0.943
Lymphocyte, (*10^9/L)	1.62 ± 0.49	1.53 ± 0.41	1.30 ± 0.48[a]	4.51	**0.014**
Monocyte, (*10^9/L)	0.40 (0.28, 0.48)	0.40 (0.36, 0.47)	0.40 (0.32, 0.49)	1.18	0.555
Platelet, (*10^9/L)	198.25 ± 52.03	193.33 ± 64.35	201.00 ± 58.85	0.11	0.893
Platelet distribution width, (fL)	15.20 (13.62, 16.47)	15.20 (13.10, 16.50)	14.80 (13.25, 16.55)	0.14	0.932
Mean platelet volume, (fL)	11.39 ± 1.16	11.54 ± 1.38	11.60 ± 1.20	0.29	0.748
NLR	2.28 (1.85, 3.04)	2.62 (2.18, 2.92)	2.70 (2.21, 5.11)	2.60	0.272
MLR	0.25 (0.18, 0.30)	0.27 (0.23, 0.32)	0.31 (0.23, 0.35)[a]	6.78	**0.034**
PLR	123.63 (89.04, 153.25)	155.91 (102.13, 171.43)	116.00 (88.56, 129.78)[b]	6.72	**0.035**
SII	468.96 (326.79, 650.65)	512.42 (410.55, 692.28)	392.00 (299.21, 606.74)	4.59	0.101
SIRI	1.03 (0.61, 1.33)	1.02 (0.90, 1.64)	1.26 (0.77, 1.80)	3.46	0.177
PNR	53.04 ± 17.59	49.51 ± 17.07	55.36 ± 21.43	0.61	0.548

CME: Cystoid macular edema; DRT: Diffuse retinal thickening; SRD: Severe retinal detachment; DR: Diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; PNR: Platelet-to-neutrophil ratio

[a]Significant difference between the group and CME group; [b]Significant difference between the group and DRT group

damage platelets, leading to their premature clearance from the circulation [17]. Additionally, the abnormal vascular endothelium in DR and DME is not conducive to the normal survival of platelets, further promoting platelet loss [18]. Neutrophils, traditionally viewed as the first line of defense in the innate immune system with pro-inflammatory roles. Elevated systemic neutrophil count has been associated with the presence and severity of DR [19]. Chronic hyperglycemia promotes neutrophil activation and recruitment to the retinal microvasculature, exacerbating inflammation and vascular leakage. Furthermore, neutrophil extracellular traps (NETs), formed by the release of chromatin and antimicrobial proteins, have been implicated in the progression of DR by promoting thrombosis and inflammation [20].

Both the decrease in platelets and the increase in neutrophils can lead to a decrease in PNR. Although there were no significant differences in the level of neutrophil and platelet between the DME group and the DR group, our findings indicated that PNR was inversely associated with the development of DME in DR patients, suggesting that chronic inflammatory conditions, as indicated by fluctuating platelet levels, may have a more significant role in DME than the acute inflammatory responses signified by neutrophil levels. However, our study did not detect a correlation between PNR and the different morphological patterns based on OCT, which may related to the limited sample size.

Our study had several inherent limitations. Firstly, it was a retrospective analysis, which was susceptible to selection bias and thus may diminish the statistical robustness of our findings. To establish causality more definitively, a prospective study with randomized control and serial measurements would be beneficial. Due to substantial missing data, the exclusion of indicators such as glycated hemoglobin from the analysis may compromise the comprehensiveness and accuracy of the study. Additionally, the study excluded patients with systemic diseases such as infections, coronary heart disease, or those taking specific medications, which could potentially result in inaccurately elevated blood parameters. Future research should encompass a larger sample size that includes these patients, allowing for separate analyses to assess their influence and to more thoroughly investigate the clinical parameters associated with DME. Despite these limitations, it was noteworthy that complete blood count measurements, including those used in our study, were commonly employed and cost-effective in daily

clinical practice. These measurements have the potential to predict the development of DME in DR patients with a high degree of sensitivity and specificity, making them valuable tools for healthcare providers.

Conclusion

Our findings suggest that PNR could emerge as a potential and economical biomarker that may contribute to the prediction of DME, with a PNR value of ≤ 68.51 demonstrating a robust association with the development of DME in patients with DR. Consequently, PNR holds promise as a valuable diagnostic tool for detecting DME, offering potential improvements in risk stratification and management strategies for DR patients. However, further research is warranted to comprehensively explore the underlying relationship between PNR and the onset of DME, as well as to validate its clinical utility in broader populations.

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Author contributions
H.S. developed the concept for the manuscript. H.S., S.L., C.P., and D.L. carried out the data collection. H.S. and Y.L. performed the data analysis and wrote the manuscript. Y.L. and X.Z. contributed to discussion. All authors contributed to the article and approved the submitted version.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol and procedures received ethical approval from the Institutional Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University [approval number: 2024(26)] and were conducted in compliance with the tenets of the Declaration of Helsinki. The requirement for informed consent was waived by the Institutional Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University because this study was based on routinely collected claims data.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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