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Exploring the correlations between six serological inflammatory markers and different stages of type 2 diabetic retinopathy

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To determine the correlations between six serological inflammatory markers, namely the systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), aggregate index of systemic inflammation (AISI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), and various stages of type 2 diabetic retinopathy (T2DR). Additionally, the diagnostic value of these markers in T2DR was evaluated. Clinical data were collected from a total of 397 patients with type 2 diabetes who visited the ophthalmology department at Mian Yang Central Hospital and the Affiliated Hospital of Southwest Medical University from January 2023 to December 2023. Based on the results of fundus photography, patients were categorized into a non-diabetic retinopathy group (NDR, $n = 121$), a non-proliferative diabetic retinopathy group (NPDR, $n = 77$), and a proliferative diabetic retinopathy group (PDR, $n = 199$). General patient information and systemic inflammatory markers, including the SII, SIRI, AIRI, NLR, PLR, and MLR, were compared among the groups, and their correlations with T2DR were analyzed. The SII values were found to be significantly higher in the PDR group compared to the NPDR group, which in turn were higher than those in the NDR group ($P < 0.05$). Similarly, the AISI values were significantly elevated in the PDR group compared to both the NPDR and NDR groups ($P < 0.05$). The SIRI and MLR values were significantly higher in the PDR group than in the NDR group ($P < 0.05$). Furthermore, the NLR and PLR values were significantly higher in the NPDR and PDR groups compared to the NDR group ($P < 0.05$). The Mantel–Haenszel chi-square test revealed a significant linear trend between the SII and PLR and the incidence of PDR ($P < 0.001$), with the incidence of PDR increasing as the quartile levels of the SII and PLR increased. Multivariate logistic regression analysis indicated that, compared with NDR, a higher SII was found to be an independent risk factor for NPDR (ORSII = 1.002, $p = 0.001$) and PDR (ORSII = 1.002, $P < 0.001$). The ROC curve analysis suggested that the combined assessment of the six inflammatory indices had the highest accuracy in the evaluation of DR, with an area under the curve (AUC) of 0.69, a sensitivity of 54%, and a specificity of 75%. The results of this study indicate that the SII is an independent risk factor for T2DR. A close correlation was observed between the SII and PLR and the occurrence and progression of T2DR. The high accuracy of the combined diagnosis of T2DR via various serological inflammatory markers underscores their potential as early biological indicators for the diagnosis of T2DR.

Keywords Systemic immune inflammation index, Systemic inflammatory response index, Aggregate index of systemic inflammation, Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Monocyte-to-lymphocyte ratio, Type 2 diabetic retinopathy

Diabetes, a group of metabolic disorders characterized by elevated blood glucose levels, has become a significant global health concern. According to research reports, the prevalence of diabetes among adults aged 20–79 years was 8.8% in 2015 and is projected to rise to 10.4% by 2040[1]. Diabetes is associated with various complications, including cardiovascular diseases, kidney diseases, and retinopathy[2]. Type 2 diabetes mellitus (T2DM), a

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common form of diabetes in adults, is primarily associated with insulin resistance and a decline in pancreatic beta-cell function[3]. T2DR, one of the most common micro-vascular complications of T2DM, is a significant cause of blindness in adults. A systematic review of population studies indicated that the annual incidence rate of diabetic retinopathy (DR) ranges from 2.2 to 12.7%[4]. The scarcity of retinal specialists poses a challenge for the early screening of T2DR. Therefore, the discovery of new biomarkers is crucial for the early identification of high-risk patients and the prevention of disease progression.

The pathophysiological mechanism of T2DR is complex, and an increasing number of studies suggest that chronic low-grade inflammation plays a significant role in its development[5]. The inflammatory response, a defensive reaction of the body to injury or infection, involves a variety of cytokines, chemokines, leukocytes, and platelets[6]. While inflammatory responses are beneficial to the body's repair and recovery to a certain extent, excessive or persistent inflammation can lead to tissue damage and organ dysfunction[7]. Patients with T2DM exhibit a state of chronic low-grade inflammation characterized by elevated levels of inflammatory factors in their blood[8]. This chronic inflammatory state leads to micro-vascular dysfunction, including damage to vascular endothelial cells, increased vascular permeability, increased blood flow resistance, and platelet aggregation[9,10], thereby promoting the onset and progression of DR.

In recent years, several new comprehensive inflammatory indices, such as the SII, SIRI, AIRI, NLR, PLR, and MLR, have been proposed. These indices utilize routine parameters from complete blood counts and integrate various leukocyte subgroups, providing a better reflection of the systemic inflammatory state in patients with T2DM[11]. Currently, various inflammation indices have been confirmed to be associated with the occurrence and prognosis of multiple diseases, including tumors, cardiovascular diseases, liver diseases, and kidney diseases[12–15]. However, the correlation between these systemic inflammatory indices and T2DR has not been fully elucidated. The present study aimed to explore the correlation between systemic inflammatory indices and T2DR and to evaluate their diagnostic value in T2DR.

Materials and methods

Experimental design

A retrospective case–control study was conducted using clinical data collected from a total of 397 patients, including 187 males and 210 females, diagnosed with type 2 diabetes at the Affiliated Hospital of Southwest Medical University and Mianyang Central Hospital from January 2023 to December 2023. The inclusion criteria for individuals were as follows: (1) aged between 18 and 80 years, and (2) diagnosed with type 2 diabetes according to the World Health Organization's 1999 diagnostic criteria for diabetes. The exclusion criteria were as follows: (1) presence of other ophthalmic diseases (such as glaucoma, macular degeneration, etc.); (2) presence of diseases that affect inflammatory markers (such as infections, tumors, autoimmune diseases, etc.); (3) presence of factors that affect the complete blood count (such as hematological diseases, transfusions, drugs, etc.). All patients underwent fundus examination and were subsequently classified into three groups according to the DR classification criteria established by the International Council of Ophthalmology in 2002: non-diabetic retinopathy (NDR), non-proliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR). This study was conducted in compliance with the principles of the Declaration of Helsinki by the World Medical Association and was approved by the hospital's ethics committee. Informed consent was obtained from all patients.

Data collection

Demographic data, including age, gender, height, and weight, were collected, and body mass index (BMI) was calculated by dividing weight by the square of height. Laboratory examinations included white blood cells (WBC), neutrophils (NE), lymphocytes (LYM), monocytes (Mo), platelets (PLT), glycated hemoglobin (HbA1c), aspartate aminotransferase (AST), alanine amino transferase (ALT), albumin (ALB), creatinine (Cr), uric acid (UA), urea, the glomerular filtration rate (eGFR), and total cholesterol (TC). The values of the inflammatory indices were calculated according to the following formulas:

$$SII = PlateletCount \times NeutrophilCount/LymphocyteCount;$$
$$SIRI = NeutrophilCount \times MonocyteCount/LymphocyteCount;$$
$$AISI = Neutrophil \times Platelet \times (Monocyte/Lymphocyte);$$
$$NLR = Neutrophil/Lymphocyte;\ PLR = Platelet/Lymphocyte;$$
$$MLR = Monocyte/Lymphocyte.$$

Statistical analysis

Statistical analysis was conducted on the collected data using SPSS 26.0 software. Measurement data conforming to a normal distribution were expressed as the mean ± standard deviation, and comparisons between groups were performed using the two independent samples t-test. For measurement data not conforming to a normal distribution, the median (interquartile range) was employed, and comparisons among multiple groups were carried out using the Kruskal–Wallis test, with post-hoc pairwise comparisons conducted via the Bonferroni test. Trend analysis was performed using the chi-square trend test through Mantel–Haenszel analysis. The analysis of influencing factors was conducted using multivariate logistic regression. The diagnostic value of each inflammatory index for DR in T2DM patients was determined through receiver operating characteristic (ROC) curve analysis, which included the calculation of the AUC. For all analyses, $P < 0.05$ was considered statistically significant.

Results

Comparison of clinical data among groups with NDR, NPDR, and PDR

The Kruskal–Wallis test and chi-square test revealed no statistically significant differences ($P > 0.05$) in the comparisons of BMI, HbA1c, AST, ALT, eGFR, TC, MO, PLT, and WBC among the three groups of patients. The proportion of males, as well as the NLR and PLR, were found to be greater in the NPDR and PDR groups compared to the NDR group ($P < 0.05$). The age of the PDR group was observed to be younger than that of the NPDR group, which was in turn younger than that of the NDR group ($P < 0.05$). ALB levels were found to be lower in the PDR group compared to the NPDR and NDR groups ($P < 0.05$). The levels of Cr, UA, Urea, NE, and AISI were observed to be greater in the PDR group compared to the NPDR and NDR groups ($P < 0.05$). LYM levels were found to be lower in the NPDR and PDR groups compared to the NDR group ($P < 0.05$). The SII values were observed to be greater in the PDR group compared to the NPDR group, which were in turn greater than those in the NDR group ($P < 0.05$). The SIRI and MLR values were found to be greater in the PDR group compared to the NDR group ($P < 0.05$) (Table 1).

Quartile ranges of the SII, SIRI, AISI, NLR, PLR, MLR, and trend tests for disease progression

Patients were classified into four groups (A-D) based on the quartile ranges of the SII, SIRI, AISI, NLR, PLR, and MLR to convert them into ordered multicategorical variables. The specific assignments were as follows: SII ("≦363.79" assigned as A, "365.25 ~ 491.25" assigned as B, "493.42 ~ 714.18" assigned as C, "≧726.05" assigned as D), SIRI ("≦0.67" assigned as A, "0.68 ~ 1.00" assigned as B, "1.01 ~ 1.47" assigned as C, "≧1.48" assigned as D), NLR ("≦1.86" assigned as A, "1.87 ~ 2.58" assigned as B, "2.59 ~ 3.47" assigned as C, "≧3.48" assigned as D), PLR ("≦96.48" assigned as A, "96.57 ~ 120.26" assigned as B, "120.42 ~ 154.85" assigned as C, "≧155.67" assigned as D), and MLR ("≦0.18" assigned as A, "0.19 ~ 0.24" assigned as B, "0.25 ~ 0.32" assigned as C, "≧0.33" assigned as D). After grouping, a significant linear trend was observed between the SII, the PLR, and the incidence of PDR ($P < 0.001$). The incidence of PDR increased as the quartile values of the SII and PLR increased. No significant trends were observed for the other indices (Tables 2 and 3).

Multivariate logistic regression analysis of clinical data for NDR, NPDR, and PDR

A multivariate logistic regression analysis was performed with the patient's disease status as the dependent variable (NDR assigned a value of 1, NPDR as 2, PDR as 3) and incorporating indicators that differed between groups as independent variables. These indicators included age, ALB, Cr, UA, urea, NE, LYM, SII, SIRI, AISI, NLR, PLR, MLR, and sex (male assigned a value of 1, female assigned a value of 2). Compared with the NDR population, being younger and male were identified as independent risk factors for NPDR (OR_{age}=0.961; OR_{gender}=3.434) ($P < 0.05$). Being younger, having lower ALB levels, having higher NE levels, and having lower

Variable	NDR (n=121)	NPDR (n=77)	PDR (n=199)	χ^2/H	P
Gender, *n*				20.321	< 0.001
Male	37 (30.6)	46 (59.7)	104 (52.3)		
Female	84 (69.4)	31 (40.3)	95 (47.7)		
Age (years)	69.00 (62.00, 74.00)	67.00 (57.00, 71.00)	55.00 (50.00, 60.00)	122.694	< 0.001
BMI(Kg/m^2)	24.44 (22.55, 26.22)	23.62 (21.75, 25.61)	23.95(21.97, 25.89)	4.011	0.135
HbA 1c (%)	7.40 (6.50, 8.80)	7.90 (6.90, 8.90)	7.90 (6.80, 9.30)	3.833	0.147
AST (U/L)	20.50 (17.70, 25.35)	20.60 (18.10, 24.90)	19.40 (16.20, 24.90)	5.336	0.069
ALT (U/L)	19.80 (14.35, 28.30)	20.00 (16.00, 26.90)	17.40 (13.30, 25.30)	5.168	0.075
ALB (g/L)	44.60 (42.45, 46.85)	44.86 (42.54, 47.11)	41.31 (35.80, 45.20)	50.703	< 0.001
Cr (μmol/L)	63.60 (54.15, 88.40)	72.10 (61.25, 88.65)	84.40 (62.60, 134.30)	27.511	< 0.001
UA (μmol/L)	327.60 (268.55, 403.00)	352.10 (276.15, 401.00)	385.00 (313.00, 446.00)	24.222	< 0.001
Urea (mmol/L)	6.49 (5.33, 7.62)	6.69 (5.31, 8.59)	7.31 (5.82, 10.81)	19.824	< 0.001
eGFR (mL/min)	88.80 (67.75, 96.30)	78.20 (64.45, 91.35)	78.20 (47.70, 100.30)	4.631	0.099
TC (mmol/L)	5.24 (4.35, 6.32)	5.03 (4.29, 6.53)	5.15 (4.45, 6.15)	0.047	0.977
NE(10^9/L)	4.06 (3.19, 5.05)	4.06 (3.38, 4.96)	4.52 (3.80, 5.31)	10.309	0.006
LYM(10^9/L)	1.89 (1.51, 2.32)	1.51 (1.17, 1.87)	1.55 (1.24, 1.90)	23.248	< 0.001
MO(10^9/L)	0.39 (0.31, 0.52)	0.36 (0.29, 0.45)	0.39 (0.31, 0.49)	2.815	0.245
PLT(10^9/L)	196.00 (164.00, 230.00)	198.00 (165.00, 228.50)	208.00 (165.00, 253.00)	5.217	0.074
WBC(10^9/L)	6.49 (5.63, 7.81)	6.39 (5.22, 7.27)	6.73 (5.76, 7.76)	4.777	0.092
SII	411.83 (295.93, 617.54)	452.80 (361.91, 711.68)	541.65 (413.82, 785.05)	30.021	< 0.001
SIRI	0.88 (0.55, 1.33)	0.95 (0.64, 1.49)	1.10 (0.77, 1.58)	13.978	0.001
AISI	168.19 (93.61, 267.94)	186.09 (124.64, 256.02)	211.47 (151.46, 358.37)	15.707	< 0.001
NLR	2.19 (1.54, 2.92)	2.57 (1.95, 3.66)	2.82 (2.14, 3.63)	28.615	< 0.001
PLR	105.76 (84.47, 135.30)	120.26 (95.79, 165.41)	127.22 (103.77, 165.66)	23.023	< 0.001
MLR	0.22 (0.16, 0.28)	0.24 (0.19, 0.32)	0.25 (0.19, 0.34)	7.971	0.019

Table 1. Comparison of clinical data among groups with NDR, NPDR, and PDR.

Mantel–Haenszel Chi-Square trend test						
Groups	A	B	C	D	Liner trend	Pearson-related
DNR	39.7%	19.0%	27.3%	14.0%	$\chi^2 = 20.84$ $P<0.001$	$R = 0.23$ $P<0.001$
NPDR	24.7%	33.8%	18.2%	23.4%		
PDR	16.6%	25.1%	26.1%	32.2%		

Table 2. SII quartile spacing and trend tests for disease progression.

Mantel–Haenszel Chi-Square trend test						
Groups	A	B	C	D	Liner trend	Pearson-related
DNR	40.5%	23.1%	23.1%	13.2%	$\chi^2 = 23.34$ $P<0.001$	$R = 0.24$ $P<0.001$
NPDR	26.0%	24.7%	19.5%	29.9%		
PDR	15.6%	26.6%	27.6%	30.2%		

Table 3. PLR quartile spacing and trend tests for disease progression.

LYM levels were identified as independent risk factors for PDR (OR_{age}=0.860; ORALB = 0.830; ORNE = 2.970; ORLYM = 0.233) ($P < 0.05$). Considering the issue of collinearity among various indicators, stepwise regression analysis was further applied to the SII, SIRI, AISI, NLR, PLR, and MLR. Compared with NDR, a higher SII was identified as an independent risk factor for NPDR (ORSII = 1.002, $p = 0.001$) and PDR (ORSII = 1.002, $P < 0.001$) (Tables 4 and 5).

ROC curve analysis of the diagnostic value of various inflammatory indices for DR

ROC curve analysis revealed that the five inflammatory indices SII, SIRI, AISI, NLR, and PLR all demonstrated diagnostic value for diabetic retinopathy, with AUCs > 0.6 and $P < 0.001$. However, the combined assessment of the six inflammatory indices provided the highest accuracy for DR, with an AUC of 0.69, a sensitivity of 54%, and a specificity of 75% (Tables 6 and 7; Figs. 1 and 2).

Discussion

An increasing number of studies have confirmed the crucial role of chronic low-grade inflammation in diabetic retinopathy[16,17]. Leukocyte extravasation, which includes neutrophils, lymphocytes, and monocytes, is currently considered the most significant characteristic of the inflammatory response. However, there is no consensus on the changes in the number of peripheral blood leukocytes and their subgroups in patients with DR. Some studies have indicated that there is no difference in the number of neutrophils and platelets in the early stages of DR, but a reduction in the number of monocytes has been observed[18]. Woo et al.[19] proposed that patients with advanced DR exhibit increased neutrophil counts in the peripheral blood. Furthermore, patients with T2DR are believed to have significantly greater monocyte counts and significantly lower lymphocyte counts compared to patients with T2DM[20]. Our study revealed that the neutrophil count in the PDR group was greater than that in the NPDR and NDR groups. The lymphocyte counts in the NPDR and PDR groups were found to be lower than that in the NDR group, with no significant difference in monocyte count among the three groups. The discrepancies between our findings and those of previous studies may be attributed to differences in sample size; hence, our research focused on composite indices.

The six indices explored in this study are novel serological inflammatory markers calculated by integrating multiple routine blood parameters, which reflects the combined effect of platelets, neutrophils, lymphocytes, and monocytes on inflammation. Our analysis revealed significant differences among the NDR, NPDR, and PDR patient groups for the aforementioned six indices. Both the SII and PLR were found to be significantly correlated with the occurrence and progression of T2DR, which is consistent with the conclusions of Gao et al.[21] The SII serves as a comprehensive indicator reflecting the status of inflammation and immunity. These results suggest the significant role of systemic inflammation in the pathogenesis of T2DR. Furthermore, an increase in the SII is associated with a clear linear trend in the incidence of PDR. This indicates that the SII may serve as a potent biomarker for predicting the occurrence and progression of T2DR. Multivariate logistic regression analysis further confirmed the status of the SII as an independent risk factor for both NPDR and PDR. This finding emphasizes the importance of monitoring changes in the SII in clinical practice, as it could aid in the early identification of patients at high risk for T2DR.

The increase in the PLR also exhibits a linear trend with the incidence of PDR, potentially reflecting the role of platelets in the pathophysiology of diabetic retinal diseases. Studies have indicated that antiplatelet therapy exerts a significant protective effect on the development of NPDR in patients with T2DM[22]. Platelets not only participate in blood coagulation but also perform functions, such as immune regulation, inflammation mediation, and vascular repair[23]. During inflammatory responses, platelets interact with neutrophils and are capable of releasing a variety of inflammatory factors[24]. These factors increase vascular permeability, promote leukocyte adhesion and migration, stimulate endothelial cell proliferation, and induce angiogenesis[25], potentially exacerbating the development of DR.

Variable	β	SE	Wald	*P*	OR	95% CI	
						Lower limit	Upper limit
NPDR	5.899	3.735	2.494	0.114			
Age	−0.040	0.018	4.938	0.026	0.961	0.928	0.995
ALB	−0.051	0.042	1.437	0.231	0.951	0.875	1.033
Cr	−0.005	0.006	0.718	0.397	0.995	0.983	1.007
UA	< 0.001	0.002	0.042	0.838	1.000	0.997	1.004
Urea	0.006	0.047	0.018	0.893	1.006	0.919	1.102
NE	−0.160	0.502	0.101	0.750	0.852	0.319	2.279
LYM	−0.699	0.685	1.041	0.308	0.497	0.130	1.904
SII	0.003	0.005	0.352	0.553	1.003	0.994	1.012
SIRI	2.505	1.502	2.781	0.095	12.239	0.645	232.296
AISI	−0.008	0.006	1.838	0.175	0.992	0.981	1.004
NLR	−0.615	0.605	1.034	0.309	0.541	0.165	1.769
PLR	0.010	0.015	0.412	0.521	1.010	0.980	1.040
MLR	−7.433	6.178	1.448	0.229	0.001	3.261E-9	107.273
Gender	Reference	Female					
Male	1.234	0.389	10.071	0.002	3.434	1.603	7.357
PDR	15.153	3.554	18.174	< 0.001			
Age	−0.151	0.019	61.522	< 0.001	0.860	0.828	0.893
ALB	−0.187	0.039	22.440	< 0.001	0.830	0.768	0.896
Cr	0.008	0.004	3.785	0.052	1.008	1.000	1.017
UA	0.003	0.002	2.189	0.139	1.003	0.999	1.006
Urea	0.044	0.038	1.308	0.253	1.044	0.969	1.125
NE	1.089	0.484	5.059	0.024	2.970	1.150	7.670
LYM	−1.456	0.675	4.648	0.031	0.233	0.062	0.876
SII	−0.002	0.004	0.296	0.586	0.998	0.989	1.006
SIRI	0.390	1.474	0.070	0.791	1.478	0.082	26.548
AISI	−0.003	0.005	0.254	0.614	0.997	0.987	1.008
NLR	−0.625	0.590	1.122	0.289	0.535	0.168	1.702
PLR	0.018	0.014	1.502	0.220	1.018	0.989	1.047
MLR	−1.349	5.912	0.052	0.819	0.259	2.406E-6	27960.707
Gender	Reference	Female					
Male	−0.108	0.368	0.086	0.769	0.898	0.436	1.847

Table 4. Multivariate logistic regression analysis of clinical data for NDR, NPDR, and PDR.

Variable	β	SE	Wald	*P*	OR	95% CI	
						Lower limit	Upper limit
NPDR	Reference	NDR					
SII	0.002	0.001	10.406	0.001	1.002	1.001	1.003
PDR	Reference	NDR					
SII	0.002	0.001	22.598	< 0.001	1.002	1.001	1.004

Table 5. Stepwise regression analysis of the SII, SIRI, AISI, NLR, PLR, and MLR.

Only the SII was statistically significant in the multivariate logistic regression analysis. However, this is considered to be due to the high collinearity among the indices, arising from the repeated use of data such as neutrophils and lymphocytes in their calculation. However, in the ROC curve analysis, the combined assessment of the six inflammatory indices demonstrated the highest accuracy for evaluating DR, with an AUC of 0.69, a sensitivity of 54%, and a specificity of 75%. These results indicate that single indices have limitations in diagnosing T2DR. By integrating multiple inflammatory indices, the diagnostic accuracy can be significantly improved. This finding provides a new direction for future research, namely, to further explore and optimize the combined assessment model of multiple indices, thereby increasing the diagnostic efficiency of T2DR.

Current research indicates that systemic inflammatory markers, such as the SII, play a significant role in the prognosis of diseases, such as cancer, infectious diseases, cardiovascular diseases, and stroke[26,27]. However, limited research has been conducted on their prognostic value in patients with DR. Researchers have found that the NLR and SII are significantly elevated in patients with diabetic macular edema (DME) complicated

	AUC	Sensitivity	Specificity	Cut-off	*P* value
SII	0.66	0.95	0.33	312.85	<0.001
SIRI	0.61	0.75	0.45	0.73	0.001
AISI	0.61	0.89	0.31	106.78	0.001
NLR	0.67	0.59	0.66	2.56	<0.001
PLR	0.65	0.82	0.41	96.60	<0.001
MLR	0.59	0.80	0.40	0.18	0.006

Table 6. ROC curve analysis of the SII, SIRI, NLR, PLR, MLR, and AISI.

	AUC	Sensitivity	Specificity	*P* value
ALL	0.69	0.54	0.75	<0.001
SII + PLR + NLR	0.66	0.45	0.83	<0.001
SII + PLR	0.68	0.47	0.84	<0.001
Except MLR	0.68	0.43	0.87	<0.001

Table 7. ROC curves for each combination of indicators.

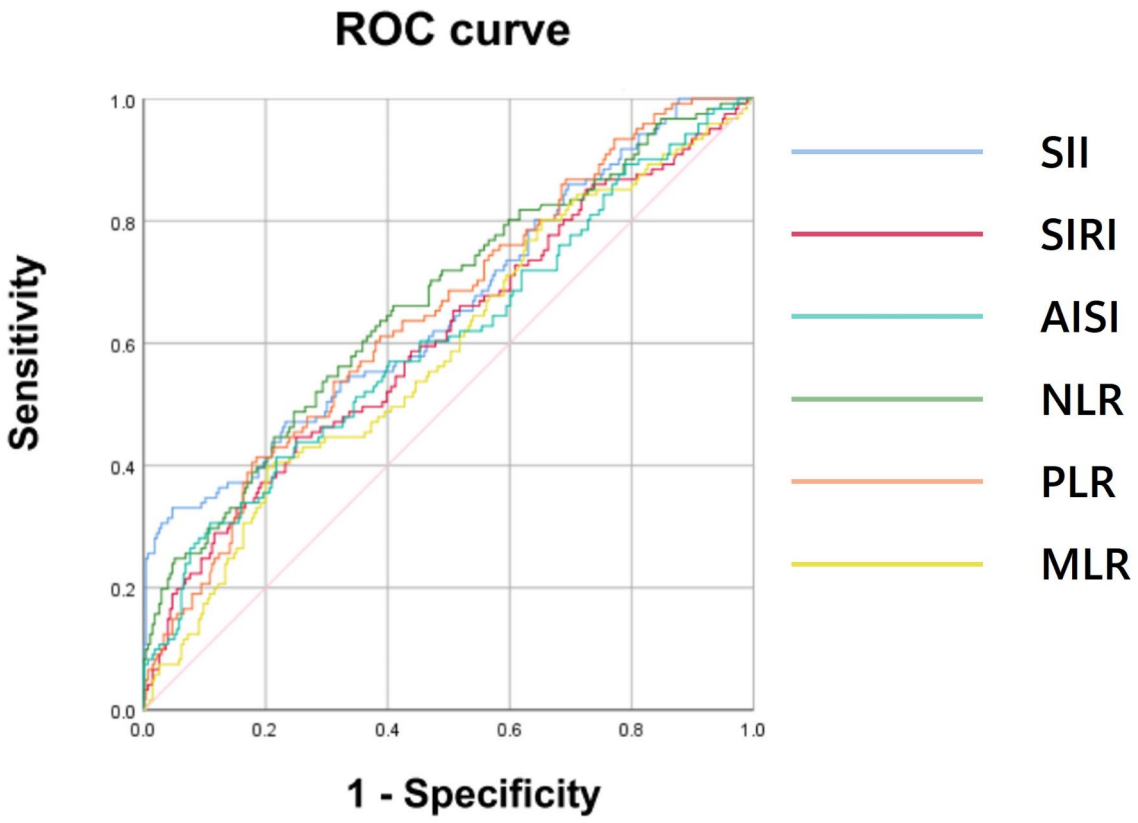

Fig. 1. ROC Curve Analysis of SII, SIRI, NLR, PLR, MLR, AISI.

by serous macular detachment (SMD), especially in late-stage cases. This suggests that the increase in systemic inflammatory mediators may be related to the high incidence of SMD[28]. Si et al. found through a retrospective analysis that elevated levels of NLR, MLR, and systemic inflammation response index (SIRI) are associated with all-cause mortality and diabetes-cardiovascular mortality in DR patients, suggesting that they may serve as independent prognostic predictors for DR[29]. Other studies have suggested that the SII has significant predictive ability for microvascular and macrovascular complications, mortality, and their combined parameters in the early stages. However, its long-term predictive value is limited[30]. In summary, incorporating systemic inflammatory markers in clinical practice can enhance the accuracy of prognosis prediction for DR patients, aiding in early

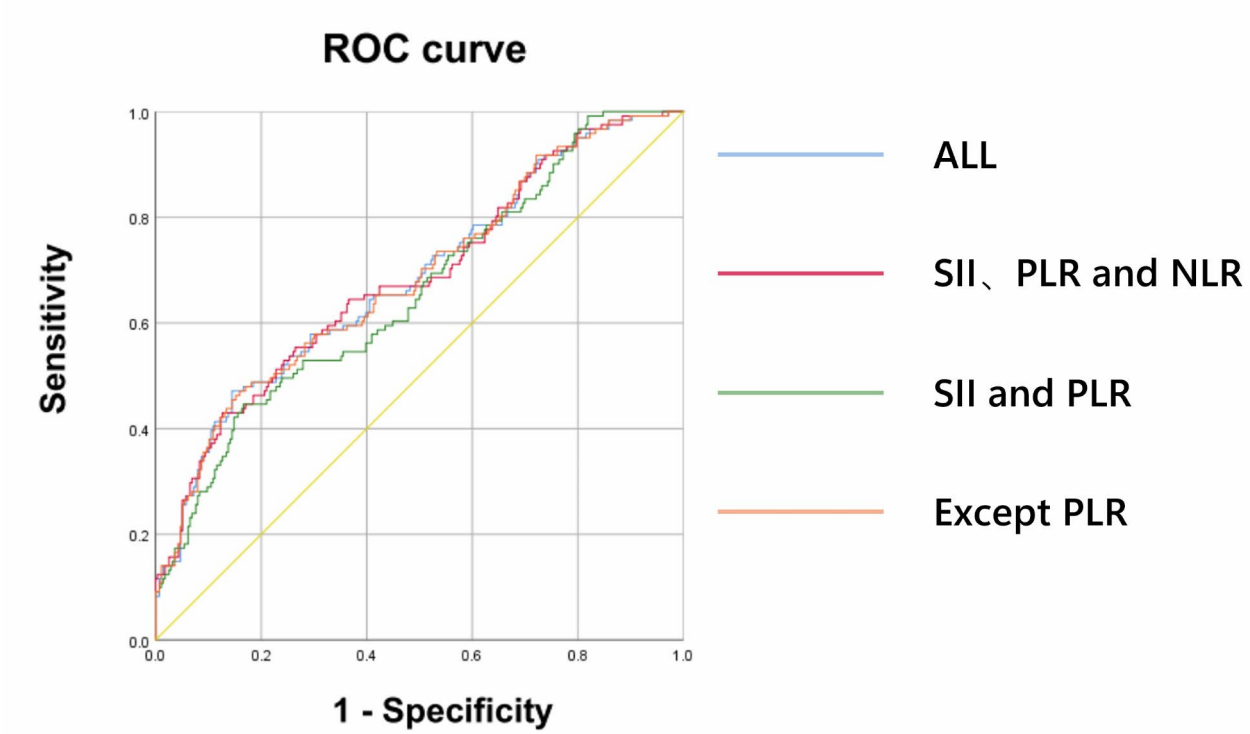

Fig. 2. ROC curves for each combination of indicators.

diagnosis and timely treatment. This approach can improve patients' quality of life and reduce healthcare costs. Therefore, it is necessary to further explore the impact of systemic inflammatory markers on the prognosis of DR patients.

Despite the valuable insights provided by this study, several limitations exist. First, this was a retrospective case-control study. Some parameters and information, such as the duration of diabetes and fasting blood glucose levels, were incomplete when patient data were collected. Second, the study included patients from only three groups, namely, the no diabetic retinopathy (NDR), NPDR, and PDR groups, without a comparison with healthy individuals. Furthermore, no follow-up observations were conducted to examine the relationships between various indicators and the prognosis of DR. Lastly, the study did not explore the specific mechanisms by which changes in each indicator contribute to the occurrence and progression of DR.

Conclusion

The present study highlights the significant roles of the SII and PLR in the occurrence and progression of T2DR. Moreover, the study demonstrates the potential of combining multiple indices to improve the diagnostic accuracy of T2DR. These findings provide novel perspectives and tools for future research and clinical practice.

Data availability

Data can be provided by the corresponding author upon reasonable request.

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Author contributions

Conceptualization, Hongbin Lv and Yan Dai; methodology, Rongjin Deng, Suhui Zhu; statistical analysis, Rongjin Deng; data curation, Bin Fan; writing—original draft preparation, Rongjin Deng; writing—review and editing, Xiaohu Chen and Yan Dai; funding acquisition, Yan Dai. All authors have read and agreed to the published version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the Affiliated Hospital of Southwest Medical University (ethics batch number: KY2024269).

Informed consent

Informed consent was obtained from all subjects involved in the study.

Additional information

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