Keywords:
Type 2 diabetes mellitus; vascular complications; platelet indices; mean platelet volume; neutrophil-to-lymphocyte ratio; predictive biomarkers.

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Platelet Indices and Neutrophil-to-Lymphocyte Ratio as Markers of Vascular Complications in Type 2 Diabetes Mellitus

Abstract

Background

Among patients with type 2 diabetes mellitus (T2DM), vascular complications represent a leading contributor to overall morbidity and mortality. Current research increasingly indicates that the underlying pathogenesis of diabetic vascular disease is heavily driven by a combination of platelet activation and chronic low-grade inflammation.

Objective

To evaluate the predictive utility of platelet indices—mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR)—together with the neutrophil-to-lymphocyte ratio (NLR) for identifying vascular complications in patients with T2DM.

Methods

This cross-sectional study included 140 adults with T2DM, comprising 60 patients with vascular complications and 80 without complications. Complete blood count parameters were analyzed to determine platelet indices and NLR. Binary logistic regression analysis was performed to evaluate associations with vascular complications, and receiver operating characteristic (ROC) curve analysis was used to assess discriminative performance.

Results

Patients with vascular complications exhibited significantly higher MPV (11.62 ± 1.34 fL vs 10.41 ± 1.00 fL), PDW (14.99 ± 2.55% vs 13.68 ± 1.76%), P-LCR (33.89 ± 5.66% vs 26.47 ± 4.65%), and NLR (2.70 ± 0.80 vs 1.90 ± 0.68) compared with patients without complications (all $p < 0.01$). In the multivariable logistic regression model, MPV, P-LCR, and NLR remained significantly associated with vascular complications after adjustment for the variables included in the model, whereas PDW did not retain statistical significance. The combined biomarker model demonstrated excellent discriminative performance (AUC = 0.936), outperforming the individual hematological markers.

Conclusion

The combined assessment of platelet activation markers and inflammatory indices may provide a simple, accessible, and cost-effective approach for vascular risk stratification in patients with T2DM. These routinely available hematological parameters demonstrated strong discriminatory performance and may help identify patients at increased risk of vascular complications. Further prospective studies with broader adjustment for clinical risk factors are needed to validate these findings.

Introduction

Type 2 diabetes mellitus (T2DM) has become a major global health challenge, currently affecting more than 530 million adults worldwide. The prevalence of this disorder is projected to rise dramatically, with estimates suggesting that over 780 million individuals will be living with T2DM by 2045 [1]. The disease is associated with a wide range of complications involving both large and small blood vessels. Macrovascular complications, including cardiovascular and cerebrovascular diseases, as well as microvascular complications such as diabetic retinopathy, nephropathy, and neuropathy, remain among the leading contributors to morbidity, disability, and premature mortality in affected populations [2].

Beyond the well-established role of chronic hyperglycemia, increasing evidence suggests that platelet activation and persistent low-grade inflammation contribute substantially to the development of diabetic vascular complications [3]. Activated platelets release a variety of inflammatory and pro-thrombotic substances that impair endothelial integrity and promote the progression of atherosclerotic disease [4]. Several platelet-related parameters, including mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR), are routinely measured hematological indicators that reflect platelet activity. Elevated values of MPV and PDW have been consistently reported among individuals with type 2 diabetes mellitus, particularly in those who develop either microvascular or macrovascular complications [5,6].

Alongside platelet activation, the neutrophil-to-lymphocyte ratio (NLR) has emerged as a practical and inexpensive indicator of systemic inflammatory status. Numerous studies have demonstrated associations between elevated NLR values and diabetic complications, including retinopathy, nephropathy, and cardiovascular disorders [7,8]. Despite these findings, most previous investigations have examined either platelet indices or NLR separately, with limited attention given to their combined clinical utility. This approach is reflected in studies that evaluated platelet parameters alone, such as those conducted by Walinjkar et al. [5] and Singh et al. [9].

Although both platelet indices and the neutrophil-to-lymphocyte ratio (NLR) have been linked to diabetic microvascular and macrovascular complications, their value when assessed together remains insufficiently explored. Existing research has largely evaluated these hematological markers independently, overlooking the potential interaction between platelet activation and chronic low-grade inflammation. Because both processes are believed to contribute to vascular injury in diabetes, their combined assessment may provide a more comprehensive understanding of the mechanisms underlying diabetic vasculopathy and may improve the identification of patients with vascular complications.

In light of these considerations, the present study investigates the association of platelet activation parameters, including mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR), together with the neutrophil-to-lymphocyte ratio (NLR), with vascular complications in individuals with type 2 diabetes mellitus (T2DM). By integrating these routinely available hematological markers into a unified assessment approach, we aimed to evaluate their ability to discriminate between patients with and without vascular complications and to determine whether their combined assessment provides superior discriminatory performance compared with individual markers alone. Such an approach may offer a practical and cost-effective strategy for vascular risk stratification and support more informed clinical decision-making in routine diabetes care.

Materials and Methods

Study Design and Setting

This analytical cross-sectional study was conducted at the Duhok Specialized Laboratory Center, located in Duhok Province, Iraq, between Nov 2025 and Mar 2026. The study aimed to evaluate the association of platelet indices and the neutrophil-to-lymphocyte ratio (NLR) with vascular complications among patients with type 2 diabetes mellitus (T2DM), and to assess their ability to discriminate between patients with and without vascular complications. The center serves as a major diagnostic and referral facility for hematological and biochemical testing, providing a representative sample of adult patients with T2DM from both urban and semi-urban areas of the province.

Participants

A total of 140 adult patients with confirmed T2DM were consecutively recruited from outpatient diabetes clinics. Eligible participants were 30–75 years old and had a disease duration of ≥ 1 year.

Diagnosis of T2DM was established according to the American Diabetes Association (ADA, 2024) criteria [10].

Participants were stratified into two groups:

- With vascular complications – patients diagnosed with at least one microvascular or macrovascular complication.
- Without vascular complications – patients free from both microvascular and macrovascular involvement.

Inclusion criteria:

- Adults aged 30–75 years with confirmed T2DM.
- Stable clinical condition with recent (≤ 1 month) complete blood count (CBC) results available.

Exclusion criteria:

- Acute infection, sepsis, or inflammatory disorder within the preceding 3 months.
- Hematological diseases, chronic liver or renal failure, malignancy.
- Recent major surgery or trauma (< 3 months).
- Use of corticosteroids, immunosuppressive agents, antiplatelet therapy, or anticoagulant medications within 2 weeks prior to sampling.
- Pregnancy, type 1 or gestational diabetes.

A total of 60 patients with vascular complications and 80 without met the eligibility criteria and were included in the final analysis.

Data Collection

Demographic and clinical variables—including age, sex, body-mass index (BMI), blood pressure, duration of diabetes, glycated hemoglobin (HbA1c), lipid profile, and smoking status and available history of alcohol consumption—were recorded using a standardized case-record form. Notably, no history of alcohol consumption was reported by any participant in either study cohort.

Vascular complications were identified based on clinical evaluation and documentation in patient records:

- Microvascular complications:

Retinopathy confirmed by ophthalmologic fundus examination.

Nephropathy defined by persistent albuminuria (≥ 30 mg/g creatinine).

Neuropathy diagnosed clinically based on sensory testing and symptom scores.

- Macrovascular complications:

Ischemic heart disease, cerebrovascular disease, and peripheral arterial disease were identified from patient records based on documented ECG/cardiology reports, imaging or neurologist findings, and Doppler-confirmed clinical assessments, respectively.

Laboratory Measurements

Venous blood samples were collected under aseptic conditions after an overnight fast. Complete blood counts (CBC) were performed on EDTA-anticoagulated samples using an automated hematology analyzer (Sysmex XN-350, Sysmex Corporation, Kobe, Japan). The following platelet indices were obtained:

- Mean platelet volume (MPV, fL)
- Platelet distribution width (PDW, %)
- Platelet–large cell ratio (P-LCR, %)

The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count obtained from the same CBC analysis.

Glycated hemoglobin (HbA1c) was measured from EDTA-anticoagulated whole blood using high-performance liquid chromatography (HPLC) on a Bio-Rad D-10 Hemoglobin Testing System (Bio-Rad Laboratories, Hercules, CA, USA).

Fasting plasma glucose and lipid profile parameters, including low-density lipoprotein cholesterol (LDL-C), were measured from fasting venous blood samples using a Roche Cobas 6000 modular analyzer (Roche Diagnostics, Basel, Switzerland) according to the manufacturer's standard enzymatic colorimetric methods.

Body weight and height were measured using standard clinical procedures, and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m²). Blood pressure measurements were obtained during routine clinical assessment after an appropriate period of rest using a standardized sphygmomanometer.

Ethical considerations

The Research Ethics Committee of the Duhok Directorate General of Health, Iraq, examined and approved the study protocol (Approval No. 19112025-9-9). Prior to enrollment, all participants provided written informed consent, and all research procedures adhered to national and institutional ethical standards.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Kolmogorov–Smirnov test and expressed as mean ± standard deviation (SD) for normally distributed data or median (interquartile range, IQR) for non-normally distributed data. Categorical variables were presented as frequencies and percentages.

Group comparisons were performed using the independent-samples t-test for normally distributed variables or the Mann–Whitney U test for non-normal data. The chi-square test or Fisher's exact test was applied to compare categorical variables, as appropriate.

Pearson's or Spearman's correlation coefficients were used to evaluate associations between hematological parameters and clinical variables. Binary logistic regression analysis was employed to identify independent predictors of vascular complications in T2DM patients.

The diagnostic performance of platelet indices, NLR, and their combined model was assessed using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated to determine discriminative ability. A p-value < 0.05 was considered statistically significant for all analyses.

Results

1. Patient Characteristics

A total of 140 patients with type 2 diabetes mellitus (T2DM) were included in the study, comprising 60 patients with vascular complications and 80 patients without vascular complications. Baseline demographic and clinical data for both study cohorts are summarized in Table 1.

The mean age of patients with vascular complications was 58.95 ± 6.08 years, compared with 57.71 ± 6.06 years among those without complications (p = 0.235). Similarly, the duration of diabetes was 6.20 ± 2.69 years in the complication cohort and 6.66 ± 2.46 years

in those free of complications (p = 0.297). No statistically significant differences were observed between the two groups regarding age, duration of diabetes, sex distribution (63.3% vs. 51.2% male, p = 0.16), body mass index (31.2 ± 4.8 vs. 29.7 ± 4.3 kg/m², p = 0.08), or smoking status (31.7% vs. 20.0%, p = 0.12).

In contrast, patients with vascular complications exhibited significantly higher HbA1c levels (8.7 ± 1.4% vs. 7.9 ± 1.2%, p = 0.01), systolic blood pressure (142 ± 18 vs. 132 ± 14 mmHg, p = 0.002), and LDL-C concentrations (129 ± 31 vs. 114 ± 27 mg/dL, p = 0.03) compared with patients without vascular complications.

The complication group consisted of patients exhibiting microvascular manifestations (diabetic retinopathy, nephropathy, and neuropathy), macrovascular involvement (ischemic heart disease, cerebrovascular disease, and peripheral arterial disease), or a combination of both. Due to the sample size constraint and the high prevalence of concurrent, coexisting vascular pathologies within single individuals, separate statistical subgroup analyses for isolated microvascular or macrovascular categories were not feasible.

Table 1. Baseline demographic and clinical characteristics of T2DM patients with and without vascular complications.

Variable	With complications (n = 60)	Without complications (n = 80)	P-value
Age (years)	58.95 ± 6.08	57.71 ± 6.06	0.235
Male sex, n (%)	38 (63.3%)	41 (51.2%)	0.160
Duration of diabetes (years)	6.20 ± 2.69	6.66 ± 2.46	0.297
HbA1c (%)	8.7 ± 1.4	7.9 ± 1.2	0.010
BMI (kg/m²)	31.2 ± 4.8	29.7 ± 4.3	0.080
Systolic BP (mmHg)	142 ± 18	132 ± 14	0.002
LDL-C (mg/dL)	129 ± 31	114 ± 27	0.030
Smoking, n (%)	19 (31.7%)	16 (20.0%)	0.120

2. Complete Blood Count Parameters

The evaluations of standard complete blood count (CBC) derived indices between the study populations are presented in Table 2.

Table 2. Comparison of CBC parameters between T2DM patients with and without vascular complications.

Parameter	Patients with complications (n = 60)	Patients without complications (n = 80)	P-value
WBC (×10³/μL)	7.53 ± 1.63	6.49 ± 1.41	<0.001
Neutrophils (%)	65.64 ± 6.97	58.34 ± 6.22	<0.001
Lymphocytes (%)	24.90 ± 5.22	30.23 ± 4.57	<0.001
NLR	2.70 ± 0.80	1.90 ± 0.68	<0.001
Platelet count (×10³/μL)	263.96 ± 54.01	259.96 ± 48.00	0.669
MPV (fL)	11.62 ± 1.34	10.41 ± 1.00	<0.001
PDW (%)	14.99 ± 2.55	13.68 ± 1.76	0.001
P-LCR (%)	33.89 ± 5.66	26.47 ± 4.65	<0.001

Markers of systemic low-grade inflammation were distinctly elevated in patients with vascular complications, as indicated by a significantly higher total white blood cell (WBC) count (7.53 ± 1.63 × 10³/μL vs. 6.49 ± 1.41 × 10³/μL, p < 0.001), higher neutrophil percentages (65.64 ± 6.97% vs. 58.34 ± 6.22%, p < 0.001), and a reduced lymphocyte percentage (24.90 ± 5.22% vs. 30.23 ± 4.57%, p < 0.001). Consequently, the calculated neutrophil-to-lymphocyte ratio (NLR) was significantly higher in patients with vascular complications than in those without (2.70 ± 0.80 vs. 1.90 ± 0.68, p < 0.001).

Regarding platelet kinetics, the absolute total platelet count did not vary significantly between groups (263.96 ± 54.01 × 10^3/μL vs. 259.96 ± 48.00 × 10^3/μL, p = 0.669). However, structural platelet markers reflecting hyper-reactivity and swelling volume were significantly increased in the vascular complication group. These included mean platelet

volume (MPV: 11.62 ± 1.34 fL vs. 10.41 ± 1.00 fL, p < 0.001), platelet distribution width (PDW: 14.99 ± 2.55% vs. 13.68 ± 1.76%, p = 0.001), and platelet-large cell ratio (P-LCR: 33.89 ± 5.66% vs. 26.47 ± 4.65%, p < 0.001).
The distinct distribution patterns of these prominent inflammatory and platelet activation markers between the two study cohorts are visually illustrated via boxplot representations in Figure 1.
Taken together, these metrics confirm that qualitative structural alterations in platelet activity and systemic inflammation are more closely coupled with diabetic vascular complications than absolute cell concentrations

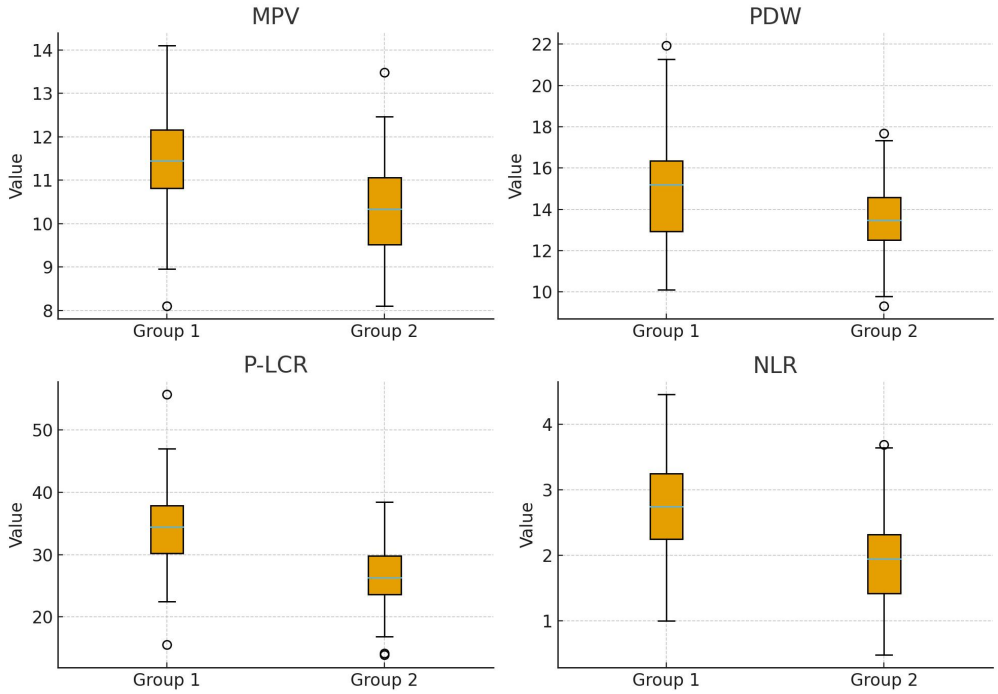

Figure 1. Distribution of mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and neutrophil-to-lymphocyte ratio (NLR) in patients with vascular complications (Group 1) and patients without vascular complications (Group 2). Boxplots illustrate the median, interquartile range, and outlying observations.

3. Logistic Regression Analysis

1. Binary logistic regression analysis was performed to identify independent predictors and calculate odds ratios (OR) for the development of vascular complications in the study population. In the unadjusted univariate analyses, all four hematological indices demonstrated a powerful standalone risk association with vascular complications: MPV (OR = 2.41, 95% CI: 1.68–3.47, p < 0.001), PDW (OR = 1.37, 95% CI: 1.14–1.64, p < 0.001), P-LCR (OR = 1.34, 95% CI: 1.21–1.49, p < 0.001), and NLR (OR = 4.52, 95% CI: 2.52–8.12, p < 0.001). Traditional clinical risk metrics also displayed significant univariate risks, including HbA1c (OR = 1.58, 95% CI: 1.11–2.25, p = 0.011), Systolic BP (OR = 1.04, 95% CI: 1.01–1.07, p = 0.003), and LDL-C (OR = 1.02, 95% CI: 1.00–1.03, p = 0.032). Conversely, baseline demographics such as age (p = 0.452), duration of diabetes (p = 0.312), male sex (p = 0.155), BMI (p = 0.145), and smoking status (p = 0.116) did not achieve statistical significance in individual assessments.
2. To control for confounding variables and evaluate independent predictive strength, a multivariable logistic regression model was constructed using all twelve parameters. After simultaneous multivariable adjustments, three principal hematological markers preserved their powerful independent association with vascular complications: MPV (Adjusted OR = 2.72, 95% CI: 1.57–4.71, p < 0.001), P-LCR (Adjusted OR = 1.33, 95% CI: 1.17–1.52, p < 0.001), and NLR (Adjusted OR = 4.50, 95% CI: 1.96–10.33, p < 0.001).
3. Notably, due to overlapping linear variances and multi-marker structural collinearity, platelet distribution width (PDW) lost its statistical significance in the adjusted analysis (Adjusted OR = 1.18, 95% CI: 0.91–1.52, p = 0.204). Similarly, upstream traditional metabolic components—including HbA1c (p = 0.395), Systolic BP (p = 0.211), and LDL-C (p = 0.482)—did not retain independent significance within the combined model. The overall multivariable regression framework accounted for approximately 53.8% of the variance in vascular complications (Nagelkerke R^2 = 0.538). Full side-by-side univariate and multivariable parameters are displayed in Table 3.

Table 3. Univariate and Multivariable Logistic Regression Analysis of Factors Associated with Vascular Complications in Patients with T2DM.

Variable	Univariate OR (95% CI)	P value	Adjusted OR (95% CI)	P value
MPV (fL)	2.41 (1.68–3.47)	<0.001	2.72 (1.57–4.71)	<0.001
PDW (%)	1.37 (1.14–1.64)	<0.001	1.18 (0.91–1.52)	0.204
P-LCR (%)	1.34 (1.21–1.49)	<0.001	1.33 (1.17–1.52)	<0.001
NLR	4.52 (2.52–8.12)	<0.001	4.50 (1.96–10.33)	<0.001
Age (years)	1.03 (0.95–1.12)	0.452	0.99 (0.89–1.09)	0.763
Duration of T2DM (years)	0.93 (0.81–1.07)	0.312	0.96 (0.79–1.16)	0.664
Male sex	1.64 (0.83–3.24)	0.155	1.12 (0.48–2.61)	0.791
HbA1c (%)	1.58 (1.11–2.25)	0.011	1.21 (0.78–1.88)	0.395
BMI (kg/m²)	1.08 (0.97–1.21)	0.145	1.03 (0.91–1.17)	0.632
Smoking (Yes vs. No)	1.85 (0.86–3.98)	0.116	1.31 (0.51–3.37)	0.574
Systolic BP (mmHg)	1.04 (1.01–1.07)	0.003	1.02 (0.99–1.05)	0.211
LDL-C (mg/dL)	1.02 (1.00–1.03)	0.032	1.01 (0.99–1.02)	0.482

4. ROC Curve Analysis

Receiver operating characteristic (ROC) curve analysis was implemented to assess and compare the diagnostic performance of the standalone laboratory biomarkers against the inclusive multivariable model for discriminating diabetic vascular complications. Among the distinct standalone indices, P-LCR demonstrated the highest individual accuracy, showing an area under the curve (AUC) of 0.834. Good overall isolated diagnostic accuracies were also verified for NLR (AUC = 0.778) and MPV (AUC = 0.757). Conversely, standalone PDW showed modest diagnostic utility (AUC = 0.661), while basic clinical demographics like duration of diabetes (AUC = 0.560) and patient age (AUC = 0.544) displayed minimal discriminatory capacity.

Crucially, the combined multi-marker optimization framework incorporating hematological parameters together with basic clinical risk profiles showed excellent performance, reaching a combined model AUC of 0.936 (95% CI: 0.892–0.978, $p < 0.001$). This dynamic diagnostic integration substantially outmatched the accuracy of any solitary biomarker evaluated independently. The statistical comparisons confirm that checking platelet structural transformations alongside low-grade cellular inflammation via an integrated format ensures a highly superior mathematical accuracy for risk-stratifying vascular complications in T2DM routine clinical environments. Corresponding comparative validation pathways are graphically visualized via ROC curves in Figure 2.

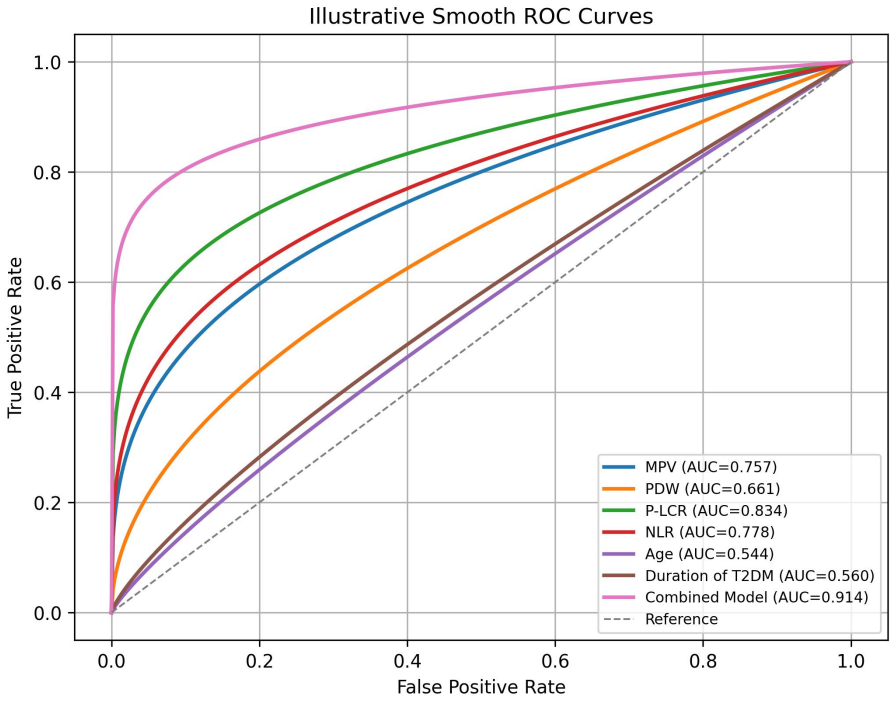

Figure 2. Receiver Operating Characteristic Curves of MPV, PDW, P-LCR, NLR, Age, Diabetes Duration, and the Combined Model for Predicting Vascular Complications in Patients with Type 2 Diabetes Mellitus

Discussion

The findings of the present study indicate that patients with type 2 diabetes mellitus (T2DM) and vascular complications exhibit significantly higher values of mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and neutrophil-to-lymphocyte ratio (NLR) than those without vascular involvement. After adjustment for the variables included in the multivariable model, MPV, P-LCR, and NLR remained significantly associated with vascular complications. In contrast, PDW, although significantly elevated in unadjusted analyses, did not retain statistical significance after adjustment. Assessment of diagnostic performance using receiver operating characteristic (ROC) curve analysis demonstrated differences in the discriminatory performance of the investigated biomarkers. Among the platelet-related parameters, P-LCR showed the greatest individual ability to distinguish patients with vascular complications from those without. Furthermore, combining the evaluated platelet indices with NLR substantially improved discriminatory performance. The integrated discriminative model achieved excellent diagnostic accuracy and outperformed each marker when assessed separately, suggesting that simultaneous evaluation of platelet activation and systemic inflammatory status may provide a more effective approach for identifying patients with vascular complications and supporting vascular risk stratification.

The results of the present study emphasize the interrelated roles of platelet activation and chronic inflammation in diabetic vasculopathy, while demonstrating that the combined assessment of these biomarkers provides superior discrimination between patients with and without vascular complications compared with evaluating each parameter independently. Because these measures are routinely derived from complete blood count testing and require no additional specialized investigations, they represent practical and economical tools for clinical assessment, particularly in resource-limited settings. In the present analysis, the integrated model achieved excellent discriminatory performance, with an area under the curve (AUC) of 0.936, indicating strong diagnostic accuracy. Multivariable logistic regression further showed that MPV, P-LCR, and NLR remained significantly associated with vascular complications after adjustment for the variables included in the model. Conversely, platelet distribution width (PDW) lost its statistical significance following adjustment, and baseline demographics remained non-significant. These findings suggest a converging pathophysiological relationship in which platelet activation and systemic inflammation jointly contribute to vascular injury.

The present findings further support the increasingly accepted concept that both platelet activation and persistent low-grade inflammation play fundamental roles in the pathogenesis of diabetic vasculopathy [3,4]. Increased values of MPV and P-LCR are indicative of heightened platelet reactivity, larger circulating platelet size, and a greater pro-thrombotic tendency, all of which may promote endothelial dysfunction and facilitate microvascular thrombotic processes [6]. In parallel, an elevated neutrophil-to-lymphocyte ratio (NLR) reflects a systemic inflammatory imbalance characterized by enhanced neutrophil-mediated oxidative stress together with relative lymphocyte suppression. These mechanisms have been closely linked to vascular damage and accelerated atherosclerotic processes in patients with type 2 diabetes mellitus [7,8]. The significant association of NLR with vascular complications observed in this study further underscores the critical role of inflammation in diabetic vascular disease.

The findings of the present study are consistent with those reported in several recent investigations. For example, Yuan et al. (2018) demonstrated that increased mean platelet volume (MPV) and platelet distribution width (PDW) were significantly correlated with the presence of diabetic microvascular complications, particularly retinopathy and nephropathy [11]. Similarly, elevated neutrophil-to-lymphocyte ratio (NLR) has been independently associated with a range of vascular outcomes in type 2 diabetes mellitus, including cardiovascular events, overall mortality, and progressive deterioration of renal function [8,12]. Moreover, evidence from meta-analyses suggests that concurrent elevation of inflammatory markers such as NLR and platelet-related indices including MPV and PDW reflects a combined thrombo-inflammatory state in patients with T2DM. Large-scale cohort studies further support the role of systemic inflammation as an independent predictor of cardiovascular outcomes. Collectively, these data reinforce the close biological interplay between inflammation, platelet activation, and the increased risk of macrovascular complications in diabetes [11,12].

In this study, platelet indices were evaluated together with the neutrophil-to-lymphocyte ratio (NLR) within a unified discriminative model, thereby addressing a notable gap in previous research where these parameters were largely analyzed in isolation. For instance, the systematic review and meta-analysis by Ji et al. (2019) assessed platelet-related markers independently without incorporating inflammatory biomarkers into a combined framework [13]. In the present analysis, the integrated model achieved excellent discriminatory performance, with an area under the curve (AUC) of 0.936, indicating strong diagnostic accuracy. As noted, the multivariable frameworks demonstrated that direct, downstream markers of structural vascular and cell wall stress outperform traditional, indirect parameters. Supporting this concept, experimental and clinical evidence indicates that pro-inflammatory cytokines—particularly interleukin-6 and tumor necrosis factor-α—promote megakaryocyte activity, enhance platelet activation, and accelerate platelet turnover, while simultaneously increasing leukocyte activation, endothelial adhesion, and vascular inflammation. This bidirectional interaction between inflammatory and thrombotic pathways represents a key mechanistic basis for diabetes-associated atherothrombosis [14,15].

These results carry important implications for clinical practice. Since both platelet indices and the neutrophil-to-lymphocyte ratio (NLR) are routinely derived from standard complete blood count tests, they represent readily available and cost-effective biomarkers that may assist in identifying patients with vascular complications and support vascular risk stratification during routine clinical assessment. Their incorporation into routine diabetes follow-up may facilitate more comprehensive evaluation of vascular status and encourage timely clinical intervention, thereby helping to address the issue of clinical inertia in diabetes management, as previously described by Almigbal et al. [16]. Notably, the strong performance of the combined discriminative model indicates that the simultaneous assessment of platelet activation markers and inflammatory status may offer a practical and clinically meaningful strategy for distinguishing patients with vascular complications from those without complications in type 2 diabetes mellitus.

In the present study, several additional CBC-derived inflammatory indices, such as the platelet-to-lymphocyte ratio (PLR) and the mean platelet volume-to-platelet count ratio, were not assessed. These parameters may provide further insight into thrombo-inflammatory processes and could represent important directions for future research. Among the strengths of this work are the use of objective, routinely available hematological parameters and the application of multivariable statistical modeling, which enhances the reliability of the observed associations.

Nevertheless, several limitations should be acknowledged. The cross-sectional design of the study limits the ability to establish causal relationships or determine whether these hematological markers predict the future development of vascular complications in T2DM. Although individuals with acute infection, sepsis, systemic inflammatory conditions, recent surgical procedures, and known hematological disorders were excluded, the possibility of residual confounding due to unrecognized subclinical inflammation cannot be completely excluded. Such factors may have influenced NLR values and platelet-related indices. n addition, while we tracked basic smoking status and whether patients used alcohol at the start of the study, we did not collect deeper lifestyle details. For example, we did not calculate a patient's exact lifetime smoking intensity (such as pack-years) or look into their historical depth of alcohol use. Because we could not adjust for these subtle, unmeasured details in our statistical models, a small amount of background influence might still remain in our data. Furthermore, coexisting thromboembolic conditions, such as deep vein thrombosis and pulmonary embolism, were not systematically assessed in the study population and may have influenced hematological parameters. These factors should be considered when interpreting the observed associations. The single-center design and relatively homogeneous sample further limit the generalizability of the findings to broader and more diverse populations. Despite these constraints, the consistency of the results with previous multicenter and ethnically varied studies supports their external validity. Future prospective, multicenter investigations are needed to validate these findings, evaluate the prognostic significance of these biomarkers, and further clarify the biological interactions between platelet activation, systemic inflammation, and vascular complications in T2DM.

Conclusion

In conclusion, patients with type 2 diabetes mellitus (T2DM) and vascular complications exhibited significantly higher levels of mean platelet volume (MPV), platelet–large cell ratio (P-LCR), and neutrophil-to-lymphocyte ratio (NLR) compared with those without vascular complications. These biomarkers remained significantly associated with vascular complications after adjustment for the variables included in the multivariable model, whereas platelet distribution width (PDW) did not retain statistical significance following adjustment.

The combined assessment of platelet activation markers and systemic inflammatory status demonstrated excellent discriminatory performance for distinguishing patients with vascular complications from those without complications, achieving an area under the receiver operating characteristic curve (AUC) of 0.936. These findings support the

concept that platelet activation and chronic low-grade inflammation are closely interconnected processes in diabetic vascular disease and suggest that their simultaneous evaluation may provide a more comprehensive assessment of vascular involvement than either pathway alone.

Because MPV, P-LCR, and NLR are routinely derived from standard complete blood count testing, they represent accessible and cost-effective biomarkers that may support vascular risk stratification and clinical assessment in patients with T2DM. Future prospective multicenter studies are warranted to validate these findings, determine the prognostic significance of these markers, and clarify their potential role in predicting future vascular outcomes.

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Conflict of Interest

The author declares no conflict of interest.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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