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Original Article

Clinical utility of hematological inflammatory indices in predicting pulmonary embolism in patients with lower extremity deep vein thrombosis

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Abstract

Aim: Despite advances in diagnostic strategies, easily accessible biomarkers that can reliably predict pulmonary embolism (PE) in patients with deep vein thrombosis (DVT) are lacking. Recently, systemic inflammatory indices, such as the systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), and aggregate index of systemic inflammation (AISI), have been investigated as potential prognostic tools. This study aimed to evaluate the predictive value and clinical applicability of these markers in identifying PE in patients with lower extremity DVT.

Material and Methods: A retrospective propensity score–matched cohort study was conducted in patients diagnosed with acute proximal lower extremity DVT. Two groups were compared: patients with isolated DVT and those with concurrent DVT and PE were compared. Propensity score matching yielded 290 patients in each group. Novel systemic inflammatory indices derived from hematological parameters (SII, SIRI, and AISI) were evaluated together with neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and traditional biomarkers (C-reactive protein (CRP) and D-dimer). Comparative analyses, logistic regression, and receiver operating characteristic (ROC) curve assessments were performed.

Results: Inflammatory indices (NLR, PLR, SII, and SIRI) and conventional biomarkers (CRP and D-dimer) were higher in the DVT and PE group compared to the isolated DVT group (all $p<0.001$). Multivariate analysis identified NLR, CRP, and D-dimer as independent predictors of PE. Receiver operating characteristic (ROC) analysis demonstrated the strongest diagnostic accuracy for CRP (AUC 0.811), followed by D-dimer (AUC 0.746) and NLR (AUC 0.735) levels.

Conclusion: Easily measurable and low-cost biomarkers, particularly NLR, along with CRP and Ddimer, provide significant predictive value for PE in patients with DVT. These parameters may support early risk stratification and assist in clinical decision-making when advanced imaging is not readily available.

Keywords: Deep vein thrombosis, pulmonary embolism, venous thromboembolism, inflammation, biomarkers

INTRODUCTION

Venous thromboembolism (VTE) is a significant global health issue characterized by high morbidity and mortality rates. It encompasses serious clinical conditions, such as deep vein thrombosis (DVT) and pulmonary embolism (PE) [1]. PE is the most severe complication of DVT and is the third leading cause of cardiovascular mortality, following myocardial infarction and stroke [2]. However, DVT is not detected in every PE case, and PE may not develop in every case of DVT [3]. The prediction of PE in patients with DVT remains difficult, as the clinical

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manifestations are nonspecific and conventional tools, such as D-dimer or scoring systems, have limited specificity. Therefore, early diagnosis and risk classification of PE are crucial for guiding therapeutic interventions. Traditional diagnostic approaches include D-dimer levels, clinical probability scores, and computed tomography pulmonary angiography (CTPA); however, these methods have limitations in terms of specificity [4].

In recent years, the pivotal role of inflammatory processes in the pathophysiology of thrombosis has become increasingly well understood. Inflammation activates the coagulation cascade and induces endothelial dysfunction, which are fundamental mechanisms that facilitate thrombus formation [5]. In this context, it has been reported that composite inflammatory indices (CII), which integrate cellular components such as neutrophils, lymphocytes, monocytes, and platelets, alongside traditional inflammatory biomarkers, quantitatively reflect systemic inflammation and possess potential diagnostic and prognostic value in clinical practice [6,7]. Currently, these indices are increasingly employed to predict the prognosis of cardiovascular diseases and thromboembolic conditions because of their ease of calculation, low cost, and noninvasive nature [8]. Furthermore, elevated levels of these indices have emerged as independent predictors of short-term mortality and complications [9,10]. However, the existing literature on the efficacy of these indices in predicting PE in patients with DVT remains limited and contains conflicting results [9,11].

This study aimed to assess the potential of systemic inflammatory indices as predictors of PE in patients with DVT. Our primary hypothesis was that these indices could serve as significant biomarkers for predicting the development of PE in patients with DVT. Consequently, our research holds the potential to contribute to the formulation of a novel algorithm to facilitate PE diagnosis and lay the groundwork for its integration into clinical decision support systems from both theoretical and practical standpoints.

MATERIAL AND METHODS

Study Design and Ethical Approval

This retrospective, propensity score-matched cohort study assessed the clinical utility of hematological inflammatory indices in predicting PE in patients with lower-extremity DVT. The study protocol was approved by the Institutional Ethics Committee (Approval No: 1-25-1536) and was conducted in accordance with the Declaration of Helsinki. Owing to the retrospective nature of the study, informed consent was not obtained. The reporting adhered to the STROBE guidelines for observational studies [12].

Study Population and Data Collection

The study was conducted from June 2019 to June 2025 at the Cardiovascular Surgery and Pulmonology Clinic of the Ankara Bilkent City Hospital. Patients diagnosed with lower-extremity DVT and/or PE were identified using the hospital's electronic medical record system and ICD-10 diagnosis codes. Initially, 1.946 patients were screened using an electronic filtering method without any subjective clinical decisions or manual interventions during patient selection. All patient data were anonymized before analysis. The study included patients over 18 years of age with no history of active infection, trauma, or surgery at the time of admission and who underwent complete laboratory tests at the time of diagnosis. Distal (infra-popliteal) DVT cases were excluded due to the heterogeneity of their clinical course and their limited association with PE [13]. Patients with active malignancy, autoimmune disease, ongoing infection, a history of active chemotherapy/radiotherapy, chronic inflammatory or hematological disease, pregnancy, and incomplete laboratory data were excluded. The diagnosis of proximal acute DVT was confirmed using duplex venous Doppler ultrasonography. PE was defined as concomitant if confirmed by CTPA within a ±48-hour window of DVT diagnosis (index date), including same-day assessments.

Group Classification and Propensity Score Matching

According to the established criteria, patients diagnosed solely with DVT and lacking imaging evidence of PE were categorized into group 1 (n=1084). In contrast, patients with concurrent DVT and PE were classified as Group 2 (n=862). To address clinical and demographic disparities between the groups, propensity score matching (PSM) was employed, using age, sex, body mass index (BMI), and diabetes mellitus as covariates. The nearest-neighbor method with a caliper width of 0.2 was applied, resulting in the inclusion of 290 patients in each group. A standardized mean difference (SMD) of less than 0.2 was deemed indicative of statistical balance. The criteria for patient selection and exclusion, the methodology for forming matched study groups, and the primary inflammatory and hematological markers analyzed are detailed in Figure 1. Data reflecting the balance before and after matching are provided in the Supplementary Material (Table S1).

Data Sources, Definitions, Variables, and Measurements

Complete blood counts (CBC), basic biochemical values, and D-dimer levels at the time of admission were retrospectively retrieved from the hospital information system. To ensure consistency across analyses, the initial venous blood samples collected at the time of diagnosis were used, thereby minimizing inter-measurement variability. The composite inflammatory indices and formulations derived from these data are shown in Figure 2.

Acute manifestations of DVT and PE were evaluated using clinical and radiological assessments. Acute proximal DVT of the lower limbs was confirmed using venous Doppler

ultrasonography, indicating the presence of a thrombus in the popliteal vein or more proximal regions such as the femoral or iliac segments. Acute PE was diagnosed in patients exhibiting at least one intraluminal filling defect in a pulmonary artery branch, as identified by CTPA. Patients diagnosed solely based on clinical suspicion were excluded.

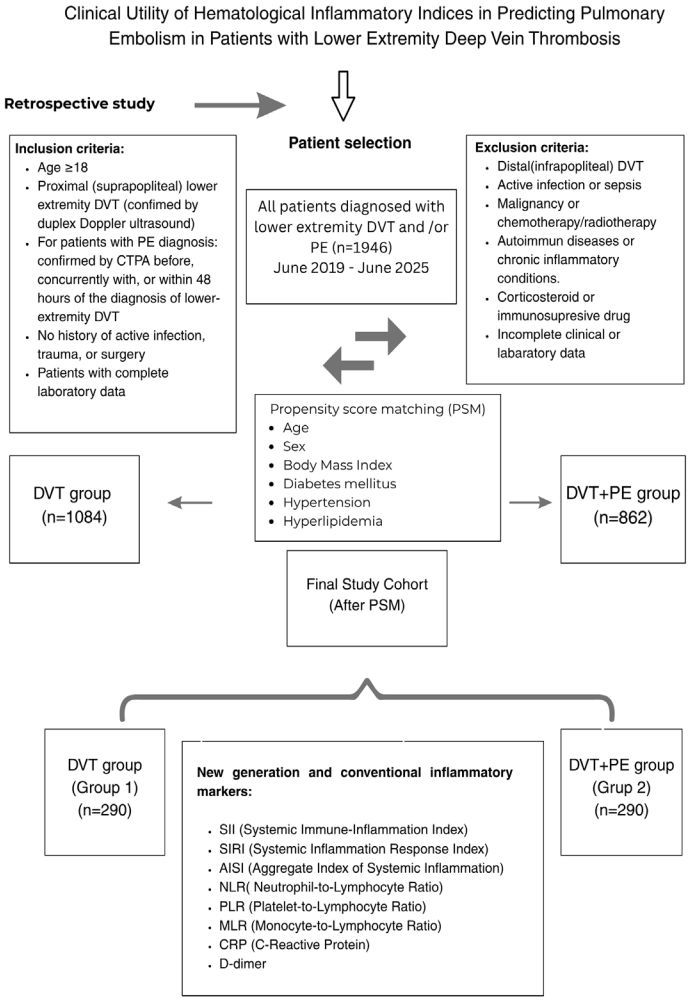

Figure 1. Flowchart of patient selection, inclusion and exclusion criteria, propensity score matching, and final study groups, along with the assessed variables.

- **Neutrophil-Lymphocyte Ratio (NLR)** = Absolute neutrophil count / Absolute lymphocyte count
- **Platelet-Lymphocyte Ratio (PLR)** = Absolute platelet count / Absolute lymphocyte count
- **Systemic Immune-Inflammation Index (SII)** = (Platelet count × Neutrophil count) / Lymphocyte count
- **Systemic Inflammation Response Index (SIRI)** = (Neutrophil count × Monocyte count) / Lymphocyte count
- **Aggregate index of systemic inflammation (AISI)** = (Neutrophil count × Monocyte count
- × Platelet count) / Lymphocyte count

Figure 2. Definitions and formulas of systemic inflammatory indices and conventional biomarkers

Risk factors were categorized as provoked or unprovoked, according to standard definitions. Prolonged immobilization was defined as reduced mobility associated with long-distance travel (air or ground) or comorbid medical conditions such as post-stroke hemiplegia. Recurrent DVT (Re-DVT) and unprovoked cases were recorded as separate categories in the database.

Statistical Methods

Data were summarized using means, standard deviations, medians, frequencies, and percentages. Categorical variables were expressed as counts and percentages, and continuous variables were expressed as mean ± SD or median. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. For intergroup comparisons, the independent sample t-test was employed for continuously distributed variables exhibiting normal distribution, the Mann–Whitney U test for non-normally distributed variables, and the chi-square or Fisher's exact test for categorical data. Receiver operating characteristic (ROC) curves were constructed to evaluate diagnostic accuracy, and the area under the curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive value were reported. Logistic regression analysis was conducted to identify independent predictors of PE. The level of statistical significance was set at $P<0.05$.

Statistical Package for the Social Sciences (SPSS) version 27.0 was used for statistical analysis. Microsoft® Excel® MSO for Microsoft 365 (Version 2503 Build 16.0.18623.20116), 64-bit for Microsoft® Visio® 2019 MSO (Version 2505 Build 16.0.18827.20102) 64-bit for graphs and images, and Canva Pro were used for flowcharts.

RESULTS

The demographic characteristics and comorbidities of both groups were compared (Table 1).

No significant differences were observed in terms of age ($p=0.087$), sex ($p=0.934$), or body mass index (BMI) ($p=0.404$). Similarly, the distribution of comorbidities was similar in both groups (all $p>0.05$).

The hematological and inflammatory parameters of both patient groups are compared in Table 2. Patients in the DVT+PE group showed significantly higher WBC, neutrophil, NLR, PLR, SII, SIRI, AISI, CRP, and D-dimer levels than those in the isolated DVT group (all $p<0.001$). Lymphocyte counts were lower in the PE group ($p<0.001$). Platelet counts were similar between the groups ($p=0.802$). Additionally, creatinine, urea, and LDH levels were significantly elevated in the PE group, whereas hemoglobin, hematocrit, and monocyte counts did not differ ($p>0.05$).

A comparison of the recurrence status, DVT etiology, risk factors, and anatomical localization between the two groups is shown in Table 3. The groups were similar in terms of DVT recurrence

(re-DVT) and according to the etiological classification of DVT (provoked/unprovoked) (p=0.338 and p=0.279, respectively). Long-term hospitalization, surgery, or trauma was more common in patients with PE than in those with isolated DVT (24.14% vs. 16.55%, p=0.023). In terms of localization, left-sided DVT was more common in the isolated DVT group (64.4% vs. 37.9%), whereas right-sided DVT was more common in the PE group (58.3% vs. 33.8%, P<0.001).

Univariate logistic regression analyses were performed to assess whether systemic inflammatory indices were independent risk factors for predicting PE development. According to the analysis results, high WBC, neutrophil count, NLR, PLR, SII, SIRI, AISI, CRP, and D-dimer values were significantly associated with PE (all p<0.05). The variables found to be significant were included in the multivariate model. Forward LR analysis identified CRP (OR 1.051, p<0.001), NLR (OR 2.048, p<0.001), and D-dimer level (OR 1.558, p<0.001) were independent predictors of PE. Monocyte levels were not statistically significant in either univariate or multivariate analyses (p>0.05) (Table 4).

In the ROC analysis performed to predict the presence of PE, the diagnostic performance of systemic inflammatory markers was examined. The ROC curves for the systemic inflammatory markers and their ability to predict PE are presented in Figure 3. The ROC analysis showed the highest diagnostic accuracy for CRP (AUC 0.811, cutoff point 46.8 mg/L, specificity 87.2%), followed by D-dimer (AUC 0.746, cutoff point 7.23 ng/ml, specificity 94.4%) and NLR (AUC 0.735, cutoff point 3.4, sensitivity 90.3%). The SII, SIRI, and AISI showed moderate discriminatory ability, whereas the PLR was less effective. Along with the AUC values obtained, the diagnostic discriminatory power and clinical performance of each marker are shown in Table 5.

Table 1. Comparison of demographic characteristics between DVT (Group 1) and DVT+PE (Group 2) Groups

Characteristics	Group 1 (n=290)			Group 2 (n=290)			P
	Mean±	SD	Median	Mean±	SD	Median	
Age	57.24±	14.20	58.50	58.97±	14.99	63	0.087
Gender							
Male	144	49.66%		145	50%		0.934
Female	146	50.34%		145	50%		
Weight	79.22±	11.42	78	77.59±	11.23	77	0.103
BMI	28.02±	4.95	26.85	27.47±	4.96	27.07	0.404
	n	**%**			**n**	**%**	**P**
HT	51	17.59%			45	15.52%	0.503
DM	32	11.03%			37	12.76%	0.521
HL	41	14.14%			39	13.45%	0.810
Chronic heart disease	38	13.10%			36	12.41%	0.791
PAD	21	7.24%			14	4.83%	0.222
CRI	18	6.21%			20	6.90%	0.737
COPD	24	8.28%			31	10.69%	0.321
Smoking	53	18.28%			60	20.69%	0.463
Immobilization	19	6.55%			14	4.83%	0.370
CVD	15	5.17%			16	5.52%	0.854

SD: Standard deviation, BMI: body mass index, HT: hypertension, DM: diabetes mellitus, HL: hyperlipidemia, PAD: Peripheral arterial disease, COPD: Chronic obstructive pulmonary disease, CRI: Chronic Renal Injury, CVD: Cerebrovascular diseases

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Table 2. Comparison of hematological and inflammatory parameters between groups

Parameter	Group 1 (n=290)			Group 2 (n=290)			P
	Mean±SD	Median	Min—Max	Mean±SD	Median	Min—Max	
WBC (x109/L)	7.85±2.43	7.34	3.75—18.96	8.63±2.53	8.25	4.55—22.71	0.000
Hemoglobin (g/dL)	12.59±2.39	12.95	5.79—16.60	12.55±2.49	13.12	5.91—16.69	0.984
Hematocrit (%)	38.67±7.64	40.30	10.80—51.30	39.01±8.10	41.20	11.70—51.30	0.296
Platelet (x10^9/L)	257.04±76.41	237.50	105.00—458.00	256.96±80.24	234.00	86.00—465.00	0.802
Neutrophil (x10^9/L)	5.92±1.73	5.67	2.28—11.05	6.99±1.58	6.52	2.76—15.76	0.000
Lymphocyte (x10^9/L)	1.85±0.85	1.63	1.08—8.90	1.53±0.16	1.53	1.16—2.08	0.000
Monocyte(x10^9/L)	0.48±0.17	0.47	0.04—0.87	0.47±0.15	0.49	0.16—0.80	0.692
AISI	429.95±251.21	385.47	31.31—1420.34	557.70±293.76	515.12	90.79—2141.42	0.000
SII	889.30±391.04	861.65	175.12—2890.46	1174.54±446.13	1075.98	347.96—3384.05	0.000
SIRI	1.69±0.86	1.66	0.13—4.35	2.16±0.87	2.14	0.62—5.71	0.000
NLR	3.53±1.31	3.37	0.86—7.34	4.62±1.20	4.41	1.68—10.22	0.000
PLR	151.33±52.45	142.72	22.92—302.99	169.73±56.99	155.63	55.13—368.64	0.000
MLR	0.29±0.12	0.27	0.03—0.59	0.31±0.11	0.31	0.09—0.62	0.000
Urea (mg/dl)	36.53±13.13	35.10	19.30—126.90	39.89±14.99	37.50	19.00—168.10	0.001
Creatinine (mg/dl)	1.06±0.33	1.04	0.59—3.78	1.14±0.40	1.12	0.55—4.43	0.000
Na (mmol/L)	137.09±2.43	136.00	130.00—143.00	136.78±4.23	137.00	126.00—153.00	0.933
Potassium (mmol/L)	4.57±0.79	4.52	2.58—7.10	4.41±0.65	4.30	2.90—6.73	0.060
LDH (U/L)	278.36±90.93	252.00	114.00—497.00	318.98±102.23	312.00	116.00—690.00	0.000
AST (U/L)	31.28±28.17	28.00	5.00—430.00	39.20±70.64	29.00	9.00—952.00	0.320
ALT (U/L)	40.02±36.69	36.00	7.00—544.00	48.14±85.91	39.00	7.00—1142.00	0.063
CRP (mg/L)	22.46±20.37	12.83	0.02—85.52	48.79±23.55	52.45	0.10—120.10	0.000
D-dimer (ng/mL)	4.92±1.87	5.33	0.05—10.40	7.37±3.18	7.77	0.78—17.13	0.000

AISI: Aggregate index of systemic inflammation, SII: Systemic inflammation index, SIRI: Systemic inflammation response index, PLR: Platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte Ratio, CRP: C-reactive protein, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, Sd: standard deviation

Table 3. Comparison of risk factors, clinical characteristics, recurrence, and side of involvement between DVT patients with and without PE

Variables	Group 1 (n=290)		Group 2 (n=290)		p
	n	%	n	%	
Recurrent DVT	7	2.41%	11	3.79%	0.338
DVT Classification by Etiology					
Unprovoked	164	56.55%	151	52.07%	0.279
Provoked	126	43.45%	139	47.93%	
Risk factors associated with DVT					
Prolonged hospitalization / surgery / trauma	48	16.55%	70	24.14%	**0.023**
Prolonged immobilization (without hospitalization)	15	5.17%	23	7.93%	0.179
Malignancy	8	2.76%	15	5.17%	0.136
Genetic factors and family history	8	2.76%	10	3.45%	0.632
Other causes	16	5.52%	25	8.62%	0.145
DVT Location (Limb Involved)					
Right lower extremity	108	37.24%	169	58.28%	<0.001
Left lower extremity	177	61.03%	110	37.93%	
Bilateral	5	1.72%	11	3.79%	
Anticoagulant use (non-DVT causes)[1]	4	1.38%	7	2.41%	0.087

DVT: Deep vein thrombosis, PE: Pulmonary embolism, Re-DVT: Recurrent deep vein thrombosis, [1]:Anticoagulant use (non-DVT causes) refers to patients already receiving anticoagulation for other medical indications (e.g., atrial fibrillation, prosthetic heart valves, prior arterial thrombosis) and is reported separately from etiological risk factor categories

Table 4. Univariate and multivariate logistic regression analyses of systemic inflammatory markers predicting PE in patients with lower extremity DVT

Variables	Univariate Model				Multivariate Model			p
	OR	95%	C. I	p	OR	95%	C. I	
Direct Hematological Indicators								
WBC	1.145	1.064	1.233	**<0.001**				
Neutrophil	1.510	1.345	1.695	**<0.001**				
Lymphocyte	0.059	0.022	0.16	**<0.001**				
Monocyte	0.794	0.289	2.185	0.655				
Inflammatory markers								
SIRI	1.913	1.554	2.356	**<0.001**				
SII	1.002	1.001	1.002	**<0.001**				
AISI	1.002	1.001	1.002	**<0.001**				
CRP(mg/L)	1.052	1.043	1.062	**<0.001**	1.051	1.040	1.061	**<0.001**
NLR	2.144	1.806	2.544	**<0.001**	2.048	1.657	2.532	**<0.001**
PLR	1.006	1.003	1.009	**<0.001**				
MLR	7.633	1.817	32.068	0.006				
DVT type								
Provoke-Unprovoked	0.835	0.602	1.158	0.279				
D-dimer (ng/mL)	1.443	1.337	1.558	**<0.001**	1.558	1.399	1.735	**<0.001**

DVT: Deep vein thrombosis, PE: Pulmonary embolism, OR: Odds ratio, CI: Confidence Interval, WBC: White blood cell, AISI: Aggregate Index of Systemic Inflammation, SII: Systemic Inflammation Index, SIRI: Systemic Inflammation Response Index, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, NLR: Neutrophil-to-Lymphocyte Ratio, CRP: C-reactive protein

Table 5. Diagnostic performance of inflammatory biomarkers for predicting pulmonary embolism in patients with DVT based on ROC curve analysis

Variables	AUC	p	95%	CI	Cut-off	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Novel systemic inflammatory indices									
SIRI	0.656	**<0.01**	0.61	0.70	2.1	53.5%	70.3%	64.3%	60.2%
SII	0.692	**<0.01**	0.65	0.73	726.2	90.0%	36.6%	58.7%	78.5%
AISI	0.638	**<0.01**	0.59	0.68	402.1	67.9%	53.8%	59.5%	62.7%
NLR	0.735	**<0.01**	0.69	0.78	3.4	90.3%	51.0%	64.9%	84.1%
PLR	0.588	**<0.01**	0.5	0.63	130.9	76.90%	38.3%	55.5%	62.4%
Traditional systemic inflammatory indices									
CRP	0.811	**<0.01**	0.78	0.85	46.9	60.00%	87.2%	82.5%	68.6%
D-dimer	0.746	**<0.01**	0.70	0.79	7.2	60.3%	94.5%	91.6%	70.4%

AUC: Area under the curve, CI: Confidence interval, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, NLR: Neutrophil-to-lymphocyte ratio, CRP: C-reactive protein

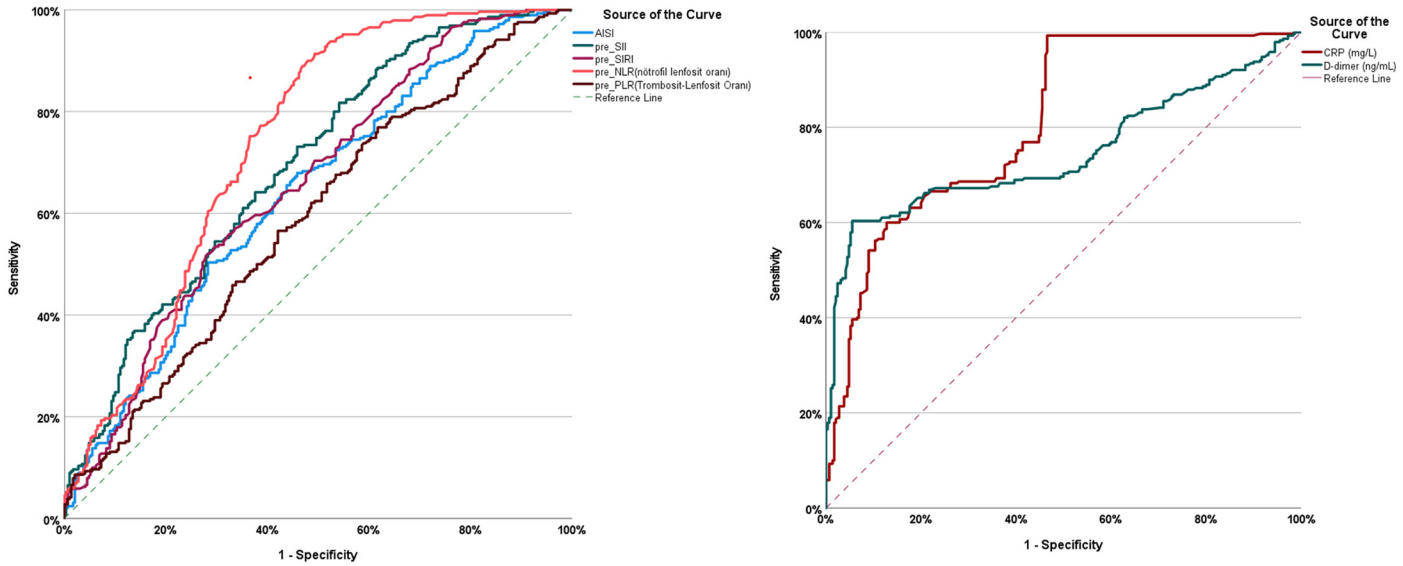

Figure 3. Receiver operating characteristic (ROC) curves of systemic inflammatory indices and conventional biomarkers for predicting pulmonary embolism in patients with DVT

DISCUSSION

VTE, which includes DVT and PE, is an increasingly significant cause of morbidity and mortality. This study systematically analyzed the diagnostic and predictive values of hematological inflammatory indices for predicting PE in patients with lower extremity DVT, along with demographic and clinical factors.

The pathophysiological link between inflammation and thrombosis is well established [14]. During thrombosis formation, neutrophils and monocytes exhibit thrombogenic effects via distinct but complementary mechanisms. Neutrophils provide the structural foundation for thrombus formation by forming Neutrophil Extracellular Traps (NETs) and triggering coagulation. In contrast, monocytes initiate the extrinsic coagulation pathway by releasing tissue factor (TF) [15]. New-generation inflammatory indices, such as the SII, SIRI, and AISI, reflect this interaction by integrating neutrophil, monocyte, and platelet activities [16]. Studies have shown that a high thrombus burden in patients with PE is associated with a worse clinical course and mortality [17].

In this study, SIRI, SII, AISI, CRP, NLR, and PLR were significantly associated with PE. In the multivariate analysis, CRP, NLR, and D-dimer levels emerged as independent predictors of PE diagnosis. The results of our multivariate analysis, performed to control for potential confounding factors and identify truly independent predictors, revealed that CRP, NLR, and D-dimer levels were independent predictors of PE diagnosis. The consistent predictive power of this combination for PE has been confirmed in multiple studies [6,18,19]. This finding highlights the potential of integrating these three parameters into clinical practice. In particular, the high sensitivity of NLR in predicting PE at values above 3.4 (90.34%) and the high specificity of CRP (87.24%) make the combined use of these two parameters attractive for clinical decision support systems.

The findings obtained in this study using ROC analysis showed that CRP level was the parameter with the highest diagnostic power. This is consistent with CRP's sensitivity of CRP to the inflammatory response and its capacity to reflect systemic inflammation associated with PE. Similarly, the literature reports that CRP levels are significantly elevated in the presence of PE and have prognostic value [20]. Although D-dimer is a marker of fibrin degradation rather than inflammation, it plays a valuable complementary role in PE diagnosis, with a specificity of 94.48%. This high specificity indicates that the negative predictive value of D-dimer is particularly important for differential diagnosis in outpatients. However, in our cohort, the D-dimer AUC value was lower than the CRP value. This finding highlights the predominant role of inflammation in the pathophysiology of PE.

In our study, the superior performance of NLR in predicting PE was noteworthy. Elevated NLR is associated with increased neutrophil activation and lymphocyte dysfunction. As an indicator of both cellular immune response and inflammatory activity, NLR has prognostic value in numerous cardiovascular and thromboembolic conditions [21,22]. Previous studies have shown that elevated NLR is strongly associated with mortality in patients with pulmonary embolism. Reported cutoff values vary across studies but generally fall within the 5–8 range [22,23]. Pooled comprehensive meta-analysis revealed a median value of 5.7 [24]. This range appears to represent the threshold at which systemic inflammation significantly contributes to poor prognosis.

Another noteworthy finding of this study is that although newer-generation-derived inflammatory indices, such as SII and SIRI, showed statistically significant associations with PE, their diagnostic performance remained lower than that of established biomarkers, such as NLR and CRP. This finding is consistent with the existing literature, which indicates that although these indices are reported at high levels in various disease groups, their discriminatory power is limited [25,26]. These findings suggest that these parameters alone are not sufficient for diagnosing PE and that more comprehensive, preferably prospective studies, are needed to determine their potential clinical benefits. In our cohort, PLR remained limited in terms of sensitivity and specificity, with a low AUC; however, some meta-analyses have reported that PLR has a more pronounced prognostic value [27]. These differences may stem from heterogeneity in thrombus burden and individual variability in inflammatory response among different study populations.

In this study, although most DVT cases were observed in the left leg, the rate of PE development was significantly higher in patients with right-sided DVT. Although large-scale multicenter studies support this finding [28,29], the current evidence remains limited. On the other hand, most existing studies have focused on proximal and distal localization rather than laterality, and data on side-specific risk remain insufficient. This relationship may be explained by anatomical and pathophysiological mechanisms, such as the possibility of faster embolization or involvement of larger venous segments [30].

According to etiological classification, unprovoked cases were more common than provoked events in both groups, although this was not statistically significant. However, when individual provoking factors were analyzed, conditions such as prolonged hospitalization, surgery, or trauma were relatively more common in patients who developed PE. However, the absence of differences between groups in terms of provoked/unprovoked PE suggests that PE may be associated not only with triggering events but also with inflammatory processes developing on a biological basis [9,31,32]. Nevertheless, these indices have also been investigated in the context of DVT recurrence, where the SII, in particular, has shown potential predictive value [33]. Although their prognostic scope may extend beyond recurrence to include outcomes such as mortality and bleeding, further prospective validation is required. Furthermore, the variability in the sensitivity and specificity of these parameters depending on patient characteristics and comorbidities raises concerns regarding their routine clinical use. Our study contributes to the literature by demonstrating the potential of both classic inflammatory markers, such as CRP and D-dimer, and new-generation-derived indices, such as NLR, SII, SIRI, and AISI, in predicting PE.

Taken together, these results provide incremental, hypothesis-generating evidence for the potential clinical utility of composite inflammatory indices in DVT-related PE risk stratification and warrant validation in larger multicenter cohorts.

Limitations

This study had several limitations. First, due to its retrospective and single-center design, it should be noted that it may be subject to observation bias in sample selection and data interpretation. Although propensity score matching was used to ensure internal balance between groups, this approach may have limited the generalizability of our results. However, although overt

infections and major inflammatory conditions were excluded and comorbidities were systematically recorded, the presence of unrecognized subclinical infection or inflammation due to low-grade comorbidity cannot be completely ruled out. The limited specificity of inflammatory markers and their potential to increase due to underlying comorbid conditions, such as infection and malignancy, require caution when interpreting the results. Furthermore, the cutoff values used in the ROC analysis were internally derived and not externally validated, which may limit their generalizability to other populations. These threshold values should be validated and optimized for different patient populations.

CONCLUSION

This study demonstrated that inflammation-based biomarkers, particularly NLR and CRP, may play an important role in predicting PE development in patients with DVT. Given their accessibility, low cost, and noninvasive nature, these parameters may provide valuable diagnostic support, particularly in settings where imaging resources are limited. Future prospective multicenter studies have the potential to generate sufficient evidence to integrate these indices into clinical guidelines.

Ethics Committee Approval: It was received from the Ethics Committee of Ankara Bilkent City Hospital (No. 1 (Approval No: 1-25-1536).

Patient Consent for Publication: This study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, informed consent forms were waived. Confidentiality of personal data was meticulously protected, and patient identities were anonymized.

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