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ORIGINAL RESEARCH

Predictive Role of Blood Cell-Derived Inflammatory Markers for the Risk of Asymptomatic Cerebral Infarction in Essential Hypertension: A Population-Based Cross-Sectional Study in Central China

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Objective: This study aimed to investigate the relationship between ACI and blood cell-derived inflammatory markers including platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) in an essential hypertensive (EH) cohort, and assess the predictive value of these inflammatory markers for ACI risk in this population.

Methods: A total of 583 EH patients were included and categorized into ACI (123 patients) and non-ACI (NACI) (460 patients) groups. Multivariate logistic regression analysis was performed to explore the relationship of PLR, NLR, SII and SIRI to ACI risk in EH population. We also used receiver operating characteristic curve analysis to assess the discriminative ability of four inflammatory markers in predicting ACI risk in EH population.

Results: ACI group exhibited higher levels of inflammatory markers (PLR, NLR, SII, and SIRI) compared to NACI group ($P < 0.05$). PLR (odds ratio (OR): 1.006, 95% confidence interval (CI): 1.001–1.011, $P = 0.023$), NLR (OR: 1.573, 95% CI: 1.225–2.021, $P < 0.001$), SII (OR: 1.002, 95% CI: 1.001–1.003, $P < 0.001$) and SIRI (OR: 1.851, 95% CI: 1.290–2.656, $P = 0.001$) were independent factors for ACI risk in EH patients. The odds ratios of the highest versus lowest quartile of PLR, NLR, SII and SIRI were 2.090 (95% CI 1.085–4.024), 3.049 (95% CI 1.509–6.161),2.464 (95% CI 1.278–4.749) and 3.372 (95% CI 1.709–6.652), respectively. PLR, NLR, SII, SIRI were characterized by area under the curve (0.586, 0.632, 0.591, 0.617) and cut-off value (125.834, 2.468, 532.011, 0.934), respectively.

Conclusion: The findings suggested that PLR, SII, SIRI, especially NLR were of significant value biomarkers to positively predict ACI risk in EH population.

Keywords: essential hypertension, platelet to lymphocyte ratio, neutrophil to lymphocyte ratio, systemic immune inflammation index, systemic inflammation response index, asymptomatic cerebral infarction

Introduction

Asymptomatic cerebral infarction (ACI) refers to intracranial infarctions detected through imaging test in patients without a documented history of stroke episodes.[1] Some patients with ACI may exhibit transient and mild symptoms such as dizziness, lightheadedness, and headaches. Due to the atypical nature of these symptoms, they have historically not received adequate medical attention. Previous studies indicated that ACI was a powerful predictor of symptomatic

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stroke, with ACI patients exhibiting a significantly higher risk of an initial stroke compared to those without ACI.[2,3] Additionally, ACI was closely associated with cognitive impairment, mental disorders, and early mortality. Many patients with ACI might ultimately develop vascular dementia.[4]

Atherosclerosis, a chronic condition with prominent inflammatory components, is the major cause of ACI.[5] Persistent hypertension can lead to vascular endothelial damage and inflammation, thus promoting atherosclerosis, and consequently increasing the risk of ACI.[6] Studies have shown that the risk of ACI is significantly higher in patients with hypertension compared to the general population, with an average prevalence of ACI among hypertensive patients ranging from 11% to 59%.[7,8] Therefore, screening for ACI risk is essential for reducing the incidence of symptomatic stroke and vascular dementia in hypertensive populations.

However, relatively expensive screening methods such as computed tomography (CT), magnetic resonance imaging (MRI), and angiography are not widely available due to limitations of economic conditions and technical capabilities. This issue is particularly pronounced in primary healthcare settings, which serve as the main battleground for medical services. Therefore, developing simpler and more economical screening or auxiliary diagnostic methods is essential for the diagnosis and tailored treatment of ACI in essential hypertensive (EH) population.

Recently identified biomarkers of systemic inflammation, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), characterized by economically friendly and readily accessible, have shown predictive capability for multiple diseases.[9–12] They have gained considerable attention in the screening of cerebrovascular diseases. For example, Xue et al found that elevated NLR levels in acute ischemic stroke (AIS) patients were significantly associated with stroke severity, short-term functional outcomes, and recurrent infarction.[13] Kocaturk et al also suggested that NLR might be a predictor of 3-months mortality in patients with AIS.[14] In a 3-year follow-up study, researchers observed that elevated PLR was associated with increased infarct volume and poorer prognosis in AIS patients.[15] Another 20-year follow-up cohort study involving 42,875 American adults indicated that elevated levels of SII and SIRI were associated with an increased risk of all-cause mortality and cardiovascular death.[16] Moreover, Xu et al identified SII as a positive predictor of stroke in middle-aged and elderly adults.[17] Zhang et al and Cai et al found that elevated SIRI was closely associated with higher mortality and severity of stroke.[18,19] These findings emphasized that the inflammatory biomarkers such as NLR, PLR, SII, and SIRI might play important role in the development and pathogenesis of cardiovascular and cerebrovascular diseases.

Whereas, previous studies have largely focused on AIS populations, with limited research available on the role of the inflammatory markers in predicting ACI risk. Furthermore, to the best of our knowledge, no studies have explored the association between these inflammatory markers including NLR, PLR, SII and SIRI and ACI specifically in EH patients. Considering the clinical predictive value of PLR, NLR, SII, and SIRI in cardiovascular and cerebrovascular diseases, the present study aims to investigate the association between these inflammatory markers and ACI in EH population, and to evaluate their predictive efficacy for ACI risk. The goal of the current study is to provide clinically applicable and cost-effective insights to inform personalized and effective treatment strategies for hypertensive patients at risk of ACI.

Materials and Methods

Study Population

A retrospective analysis was conducted and 583 EH patients hospitalized in the hypertension department of Henan Provincial People's Hospital from January 1, 2024, and May 31, 2024, were included. Based on the presence of ACI, patients were divided into an ACI group (123 cases) and a non-ACI (NACI) group (460 cases).

Inclusion criteria required that participants meet all of the following conditions: (a) age ≥18 years; (b) diagnosed as EH, based on the guidelines for the prevention and treatment of hypertension;[20] (c) completion of cranial CT or MRI imaging for ACI. Exclusion criteria required that participants meet any of the following conditions: (a) secondary hypertension; (b) coronary heart disease or rheumatic heart disease; (c) symptomatic cerebral infarction or cerebral hemorrhage; (d) autoimmune diseases or neuroendocrine disorders; (e) acute or chronic infection; (f) severe pulmonary or renal dysfunction; (g) use of anticoagulant or antiplatelet medications.

Clinical and Biochemical Assessment

General data were collected for all patients, including age, blood pressure, height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), duration of hypertension. Venous blood samples were obtained from each participant after at least 10 hours of fasting.

Blood cell count (white blood cell, neutrophil, lymphocyte, monocyte, platelet), renal function (creatinine, uric acid), lipid profile (total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol), glycated hemoglobin and homocysteine were measured by a specialized team in the hospital's central laboratory. Calculations for body mass index (BMI), NLR, PLR, SII, and SIRI were calculated by the following formulas: BMI = weight (kg)/height (m^2), NLR = neutrophil count/lymphocyte count, PLR = platelet count/lymphocyte count, SII = (neutrophil count × platelet count)/lymphocyte count, and SIRI = (neutrophil count × monocyte count)/lymphocyte count.

Diagnostic Criteria

The diagnostic criteria for ACI required that patients have no history of previous stroke or transient ischemic attack (TIA), with cranial MRI or CT imaging showing infarct or softening lesions consistent with cerebrovascular distribution, but without corresponding neurological symptoms or localized signs.[3]

The diagnostic criteria for hypertension required SBP ≥140 mmHg and/or DBP ≥90 mmHg measured three times on separate days in the absence of antihypertensive medication, or a history of hypertension with current antihypertensive treatment.[20]

Statistical Analysis

Statistical analyses and figure generation were performed using SPSS version 22.0, R version 4. 2.2 and GraphPad Prism 9, respectively. Continuous data with normal distribution are presented as mean ± standard deviation and were compared between groups using an independent samples *t*-test. Non-normally distributed continuous data are expressed as median (inter-quartile range) and were compared between groups using the Mann–Whitney *U*-test. Categorical data were analyzed with the χ^2-test. Correlations were evaluated using the Spearman method. Multivariate logistic regression analysis was employed to assess the association of ACI with the selected factors. The models were adjusted for the potential confounders which exhibited statistically significant variations while comparing baseline demographics and clinical characteristics between the two groups. Receiver operating characteristic (ROC) curves were conducted to evaluate the predictive capability of NLR, PLR, SII, and SIRI for ACI risk in EH patients. Net reclassification improvement (NRI) was conducted to further assess the predictive performance. Statistical significance was set at a two-sided $P < 0.05$.

Results

Comparison of Demographic and Clinical Characteristics

A total of 583 EH patients were included in the current study and classified into ACI group with 123 cases and NACI group with 460 cases, accounting for an ACI prevalence of 21.10%. Age, systolic blood pressure, duration of hypertension, glycated hemoglobin, PLR (Figure 1A), NLR (Figure 1B), SII (Figure 1C), and SIRI (Figure 1D) of patients in the ACI group were significantly higher than that of patients in the NACI group ($P < 0.05$). Diastolic blood pressure and lymphocyte levels of patients were significantly lower in the ACI group than that of patients in the NACI group ($P < 0.05$, Table 1).

Correlation between ACI and Clinical and Biochemical Indicators

To explore the correlation between ACI and clinical and biochemical indicators, Spearman correlation analysis was conducted. The results showed that ACI was positively correlated with age, systolic blood pressure, duration of hypertension, glycated hemoglobin, NLR, PLR, SII, and SIRI, while being negatively correlated with diastolic blood pressure and lymphocyte count at significant levels ($P < 0.05$) (Table 2).

Association of ACI With Inflammatory Biomarkers

The unadjusted logistic regression model showed that NLR (OR 1.688; 95% CI: 1.370–2.079, $P < 0.001$), PLR (OR 1.007; 95% CI: 1.003–1.012, $P = 0.002$), SII (OR 1.001; 95% CI: 1.001–1.002, $P < 0.001$), and SIRI (OR 1.830; 95% CI:

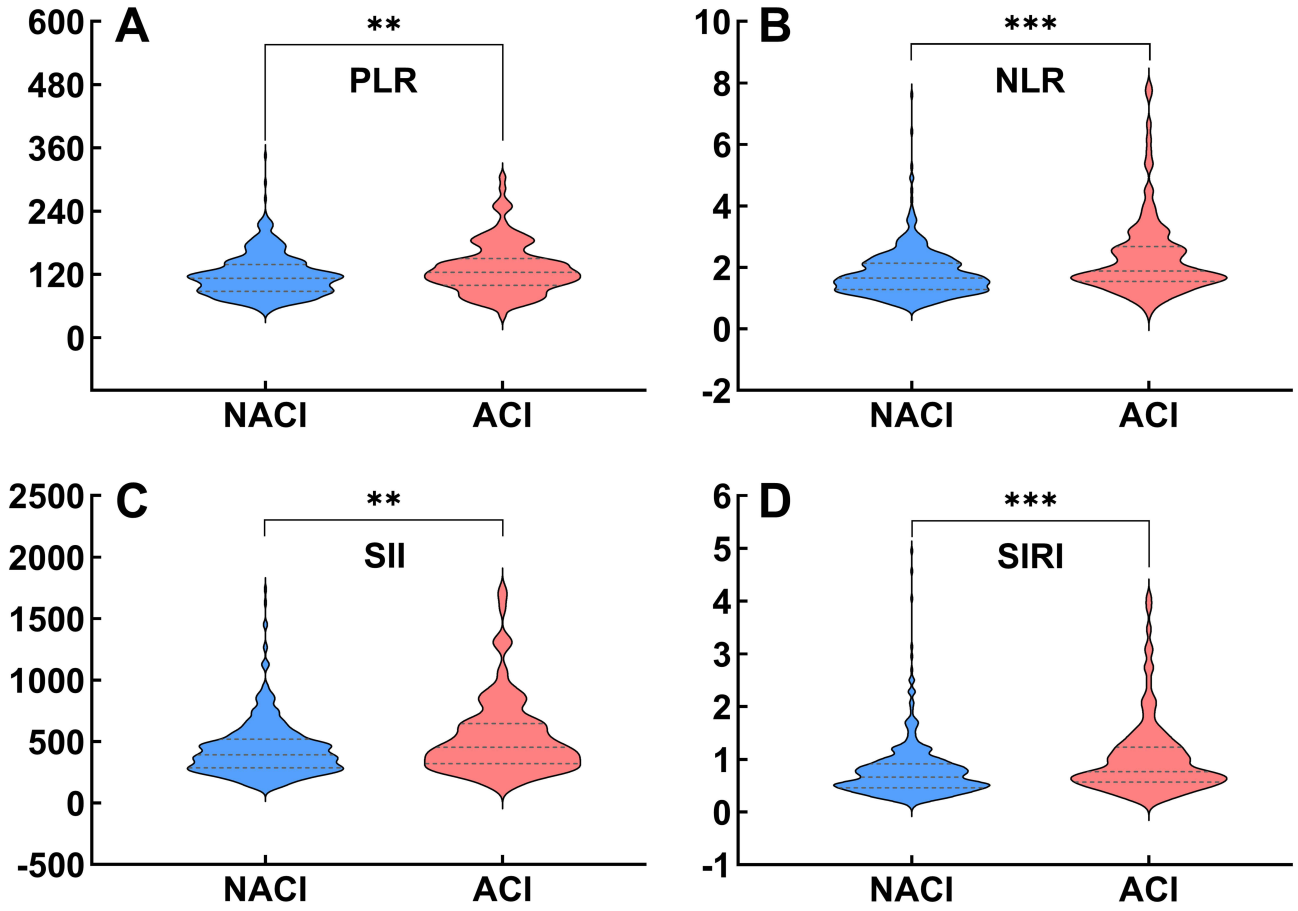

Figure 1 The distribution of inflammatory biomarkers (PLR, NLR, SII, and SIRI) in violin plot. (**A**) Comparison of PLR between NACI and ACI groups; (**B**) Comparison of NLR between NACI and ACI groups; (**C**) Comparison of SII between NACI and ACI groups; (**D**) Comparison of SIRI between NACI and ACI groups.
Abbreviations: ACI, Asymptomatic Cerebral Infarction; NACI, No ACI; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index; ** and *** indicate $P < 0.01$ and $P < 0.001$, respectively.

1.346–2.489, $P < 0.001$) were identified as risk factors for ACI in EH patients. After adjusting for confounding variables including age, duration of hypertension, systolic blood pressure, diastolic blood pressure and glycated hemoglobin, all the four inflammatory biomarkers including NLR (OR 1.573; 95% CI: 1.225–2.021, $P < 0.001$), PLR (OR 1.006; 95% CI:

Table 1 Comparison of Baseline Characteristics and Laboratory Parameters of the Study Population

Variables	NACI (n=460)	ACI (n=123)	*P*
Clinical Characteristics			
Age(y)	45.42±14.37	57.91±13.31	<0.001
Male(%)	283(61.5)	75(61.0)	0.912
BMI	26.62±3.84	26.16±3.21	0.221
SBP (mmHg)	147.96±18.89	152.66±21.13	0.018
DBP (mmHg)	90.52±15.35	86.7±16.15	0.016
Duration of Hypertension(y)	2.0(0.17,6.75)	6.00(1.00,14.00)	<0.001

(*Continued*)

Table 1 (Continued).

Variables	NACI (n=460)	ACI (n=123)	*P*
Biochemical characteristics			
TC(mmol/L)	4.53±0.96	4.37±1.01	0.095
TG(mmol/L)	1.51(1.1, 2.2)	1.44(1.09, 2.17)	0.619
HDL-C(mmol/L)	1.18±0.24	1.16±0.25	0.537
LDL-C(mmol/L)	2.72±0.78	2.59±0.82	0.102
SCr (μmol/L)	61.0(52.0,73.0)	62.5(52.0, 75.0)	0.194
UA (mmol/L)	356.89±98.76	351.12±97.98	0.570
HbA1c (%)	5.73±0.85	6.19±1.07	<0.001
HCY (mmol/L)	11.60(9.9,14.55)	12.4(10.03,14.98)	0.225
WBC count(10^9/L)	6.35(5.30,7.47)	6.46(5.29,7.61)	0.583
Neutrophil count (10^9/L)	3.55(2.82,4.33)	3.8(2.94,4.74)	0.054
Lymphocyte count (10^9/L)	2.09(1.75,2.57)	1.8(1.53,2.34)	<0.001
Monocyte count (10^9/L)	0.39(0.32,0.49)	0.41(0.35,0.52)	0.092
Platelet count (10^9L)	237(202.25,276)	229(183,268)	0.183

Abbreviations: ACI, asymptomatic cerebral infarction; NACI, No ACI; BMI, body mass index, SBP, systolic blood pressure, DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BUN, blood urea nitrogen; UA, uric acid; SCr, serum creatinine; HCY, homocysteine; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

1.001–1.011, $P = 0.023$), SII (OR 1.002; 95% CI: 1.001–1.003, $P < 0.001$), and SIRI (OR 1.851; 95% CI: 1.290–2.656, $P = 0.001$) were identified as independent risk factors for ACI in EH patients (Table 3).

Multivariate logistic regression analysis based on quartile of NLR, PLR, SII, and SIRI was conducted as shown in Table 4. After adjustment for confounding factors same as used in Table 3, NLR (with quartile 1 (Q1) as reference, adjusted OR of quartile 2 (Q2): 2.258, 95% CI:1.082–4.710; adjusted OR for quartile 4 (Q4): 3.049, 95% CI: 1.509–6.161; P for

Table 2 The Correlation Between ACI and the Clinical and Biochemical Characteristics

Clinical and Biochemical Characteristics	r	*P*	Clinical and Biochemical Characteristics	r	*P*
Age(y)	0.336	<0.001	HbA1c (%)	0.224	<0.001
BMI (kg/m^2)	−0.042	0.309	HCY (mmol/L)	0.056	0.225
SBP (mmHg)	0.083	0.048	WBC count(10^9/L)	0.023	0.583
DBP (mmHg)	−0.113	0.007	Neutrophil count (10^9/L)	0.08	0.054
Duration of Hypertension(y)	0.198	<0.001	Lymphocyte count (10^9/L)	−0.164	<0.001
TC (mmol/L)	−0.067	0.111	Monocyte count (10^9/L)	0.07	0.092
TG (mmol/L)	−0.021	0.635	Platelet count (10^9/L)	−0.055	0.184

(*Continued*)

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Table 2 (Continued).

Clinical and Biochemical Characteristics	r	*P*	Clinical and Biochemical Characteristics	r	*P*
HDL-C (mmol/L)	−0.025	0.547	PLR	0.122	0.003
LDL-C (mmol/L)	−0.066	0.118	NLR	0.187	<0.001
SCr (μmol/L)	0.054	0.194	SII	0.129	0.002
UA (mmol/L)	−0.028	0.503	SIRI	0.165	<0.001

Abbreviations: BMI, body mass index; SBP, systolic blood pressure, DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BUN, blood urea nitrogen; UA, uric acid; SCr, serum creatinine; HCY, homocysteine; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

Table 3 Multiple Logistic Regression Analysis of the Association of the Inflammatory Biomarkers With ACI

Inflammatory Indexes	Crude		Adjusted	
	OR (95% CI)	*P*	OR (95% CI)	*P*
PLR	1.007(1.003,1.012)	0.002	1.006(1.001,1.011)	0.023
NLR	1.688(1.370,2.079)	<0.001	1.573(1.225,2.021)	<0.001
SII	1.001(1.001,1.002)	<0.001	1.002(1.001,1.003)	<0.001
SIRI	1.830(1.346,2.489)	<0.001	1.851(1.290,2.656)	0.001

Abbreviations: PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

trend < 0.05), SII (with Q1 as reference, adjusted OR for Q4: 2.464, 95% CI: 1.278–4.749; P for trend < 0.01), and SIRI (with Q1 as reference, adjusted OR for Q4: 3.372, 95% CI: 1.709–6.652; P for trend < 0.01) were significantly associated with ACI in EH patients. For PLR, compared to Q1, the adjusted OR for Q4 was 2.090 (95% CI:1.085–4.024, $P < 0.05$), although the overall P trend was not statistically significant ($P = 0.140$).

Table 4 Multivariate Logistic Regression Analysis According to Quartile of PLR, NLR, SII, and SIRI

Variable	n	ACI	Crude		Adjusted	
			OR (95% CI)	*P*	OR (95% CI)	*P*
PLR						
Q1(< 89.94)	146	23(15.8)	1.000(1.000, 1.000)	Ref.	1.000(1.000, 1.000)	Ref.
Q2(89.94–115.22)	146	27(18.5)	1.213(0.659, 2.234)	0.535	1.259(0.626, 2.533)	0.519
Q3(115.22–141.72)	146	33(22.6)	1.562(0.865, 2.819)	0.139	1.582(0.793, 3.156)	0.193
Q4(≥141.72)	145	40(27.6)	2.037(1.146, 3.621)	0.015	2.090(1.085, 4.024)	0.027
P for trend				0.077		0.140

(*Continued*)

Table 4 (Continued).

Variable	n	ACI	Crude		Adjusted	
			OR (95% CI)	*P*	OR (95% CI)	*P*
NLR						
Q1(<1.31)	146	17(11.6)	1.000(1.000, 1.000)	Ref.	1.000(1.000, 1.000)	Ref.
Q2(1.31–1.71)	146	29(11.6)	1.881(0.983, 3.599)	0.056	2.258(1.082, 4.710)	0.030
Q3(1.71–2.24)	146	28(19.2)	1.801(0.938, 3.457)	0.077	2.036(0.972, 4.265)	0.059
Q4(≥ 2.24)	145	49(33.8)	3.873(2.101, 7.14)	<0.001	3.049(1.509, 6.161)	0.002
P for trend				<0.001		0.020
SII						
Q1(<289.04)	146	24(16.4)	1.000(1.000, 1.000)	Ref.	1.000(1.000, 1.000)	Ref.
Q2(289.04–402.24)	146	28(19.2)	1.206(0.661, 2.200)	0.541	1.263(0.634, 2.516)	0.506
Q3(402.24–549.73)	146	25(17.1)	1.05(0.568, 1.941)	0.876	1.238(0.618, 2.479)	0.546
Q4(≥ 549.73)	145	46(31.7)	2.362(1.349, 4.136)	0.003	2.464(1.278, 4.749)	0.007
P for trend				<0.001		0.033
SIRI						
Q1(<0.48)	146	19(13.0)	1.000(1.000, 1.000)	Ref.	1.000(1.000, 1.000)	Ref.
Q2(0.48–0.69)	146	30(20.5)	1.729(0.923, 3.237)	0.087	1.606(0.797, 3.237)	0.185
Q3(0.69–0.98)	146	25(17.1)	1.381(0.724, 2.636)	0.328	1.594(0.766, 3.317)	0.213
Q4(≥0.98)	145	49(33.8)	3.412(1.887, 6.169)	<0.001	3.372(1.709, 6.652)	<0.001
P for trend				<0.001		0.004

Abbreviations: ACI, asymptomatic cerebral infarction; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

Predictive Value of the Inflammatory Biomarkers for ACI Risk

To evaluate the predictive efficiency of PLR, NLR, SII, and SIRI for ACI in EH patients, ROC curves were plotted. As shown in Figure 2 and Table 5, the area under the curve (AUC) values for PLR, NLR, SII, and SIRI were 0.586 (95% CI: 0.529–0.644), 0.632 (95% CI: 0.576–0.689), 0.591 (95% CI: 0.532–0.650), and 0.617 (95% CI: 0.560–0.674), respectively. The optimal cutoff points were 125.834 for PLR (sensitivity 49.6%, specificity 66.7%), 2.468 for NLR (sensitivity 34.1%, specificity 86.7%), 532.011 for SII (sensitivity 39.8%, specificity 76.5%), and 0.934 for SIRI (sensitivity 43.9%, specificity 77.2%). Furthermore, the NRI [95% CI: 0.200 (0.002–0.397), $P = 0.047$] for ACI was significantly improved by the addition of NLR to the basic model.

Discussion

The current study was based on a cohort of 583 EH patients (with an ACI prevalence of 21.10%) and, for the first time to our best knowledge, explored the association of EH combined with ACI with PLR, NLR, SII and SIRI. Results showed that PLR, NLR, SII, and SIRI levels were significantly elevated in the ACI group than that in the NACI group and positively correlated with ACI. After adjusting for confounding variables (age, duration of hypertension, systolic blood pressure, diastolic blood pressure, and glycated hemoglobin), multivariate logistic regression analysis indicated that PLR, NLR, SII, and SIRI were independent risk factors for ACI, demonstrating their potential of predictive value for ACI risk in EH population. Further ROC curve analysis revealed that the AUC values for these inflammatory indicators were all above

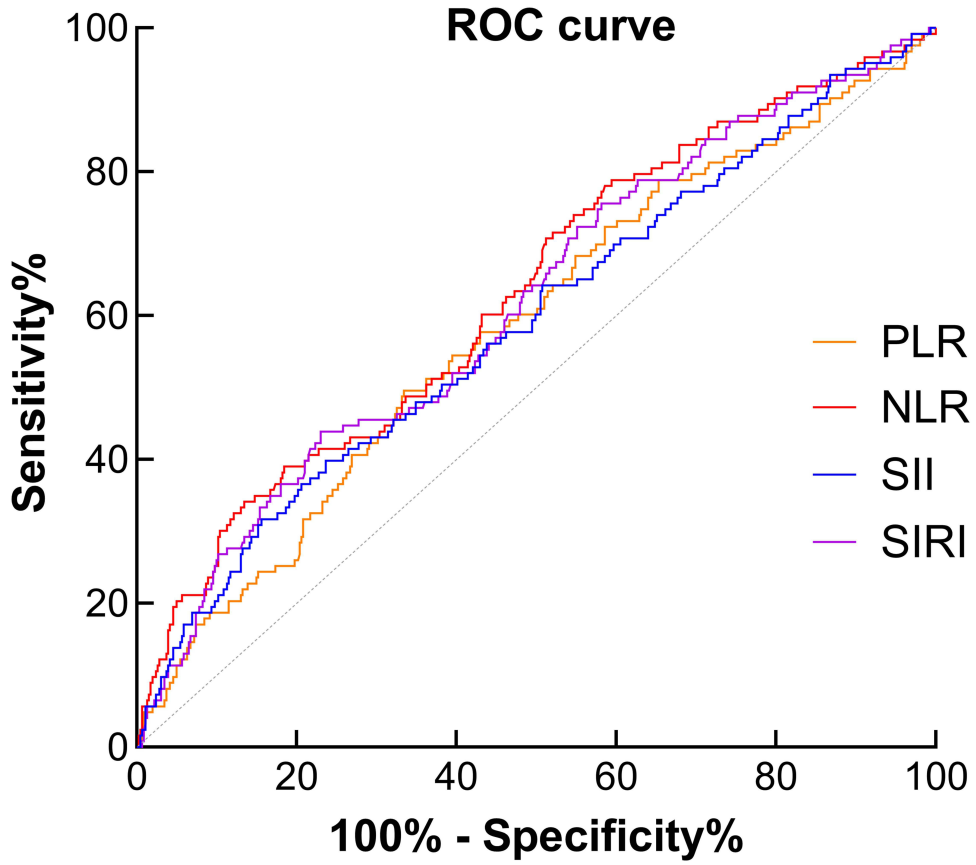

Figure 2 Receiver operating characteristic curve for inflammatory biomarkers (PLR, NLR, SII, and SIRI) to predict ACI outcome.
Abbreviations: PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

0.500, with the ranking from highest to lowest as follows: NLR > SIRI > SII > PLR. This suggested that PLR, SII, and SIRI, especially NLR, could provide a cost-effective, convenient, and efficient detection method to assist in screening EH patients at high risk for ACI, thus increasing the detection rate of ACI complications in EH population while substantially reducing the high costs and low efficiency associated with blind screening.

Atherosclerosis, a chronic inflammatory disease prevalent in hypertensive patients, is the primary cause of cardiovascular and cerebrovascular diseases. Inflammatory response involving leukocytes and their subtypes (neutrophils, monocytes, and lymphocytes) as well as platelets playing a critical role in the atherosclerosis process motivated by the mechanisms including oxidative stress, hypoxia, and vascular endothelial injury. Neutrophils can secrete a large number of inflammatory mediators, chemokines, and reactive oxygen species, inducing endothelial cell damage, consequently

Table 5 ROC Analysis of the Capability of PLR, NLR, SII and SIRI to Predict the Risk of ACI

Variables	AUC	*P*	95% CI	Se (%)	Sp (%)	Cutoff
PLR	0.586	0.003	0.529–0.644	49.60	66.70	125.834
NLR	0.632	<0.001	0.576–0.689	34.10	86.70	2.468
SII	0.591	0.002	0.532–0.650	39.80	76.50	532.011
SIRI	0.617	<0.001	0.560–0.674	43.90	77.20	0.934

Abbreviations: AUC, area under curve; CI, confidential interval; Se, sensitivity; Sp, specificity; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; SII, systemic immune inflammation index; SIRI, systemic immune inflammation response index.

disrupting normal vasculature and leading to ischemia and hypoxic necrosis.[21] Net-like DNA structures, originating from neutrophils and wrapped with various bioactive enzymes, could stimulate platelet adhesion, subsequently leading to thrombosis formation.[22,23] Monocytes played a crucial role in the formation and rupture of atherosclerotic plaques. Monocytes can be activated once adhered to the endothelium and, under the influence of cytokines, differentiate into various types of macrophages which then transform into foam cells. These foam cells accumulate to form fatty streaks which then developed into fibrous plaques, thereby promoting the formation of atherosclerotic lesions.[24–26] Additionally, Monocyte-macrophages could contribute to an increased risk of plaque rupture by secreting various tissue factors, growth factors, and inflammatory mediators.[27] Platelets are central to the process of thrombosis formation, as they could form thrombi in conjunction with fibrin. Activated platelets can also release numerous inflammatory mediators, inducing the expression of tissue factors, triggering the coagulation cascade, leading to the generation of thrombin and further activation of platelets, ultimately resulting in thrombosis.[28,29] Furthermore, platelets can influence the biological behavior of leukocytes by mediating the recruitment and adhesion of neutrophils, monocytes, and other cells to the vascular endothelium, thereby affecting the progression of vascular lesions.[30] In contrast, lymphocytes played an inhibitory role in atherosclerosis process.[31] A reduction of lymphocyte can accelerate the formation of necrotic lipid cores in coronary atherosclerotic plaques, increasing the plaque burden, weakening the fibrous cap, and contributing to plaque rupture.[32] The oxidized low-density lipoprotein receptors present on lymphocytes can intervene in the atherosclerotic process and prevent the occurrence of atherosclerosis.[33] Previous studies have provided substantial cytological evidence supporting that neutrophils, monocytes, platelets, and lymphocytes are closely linked to the pathogenesis of cardiovascular and cerebrovascular diseases, highlighting their importance in ischemic disease development. Therefore, it is inferred that PLR, NLR, SII, and SIRI, which are composed of these blood cell-related indices, might also be closely associated with ACI, a cerebrovascular disease.

PLR, NLR, SII, and SIRI integrate the combined effects of neutrophils, monocytes, platelets, and lymphocytes in the pathogenesis of atherosclerosis. These inflammatory biomarkers not only possess the advantages including simplicity, non-invasiveness, low cost, easy accessibility and reproducibility, similar to the individual cell counts, but they also demonstrate greater stability and are less influenced by extraneous factors. Previous studies have established close correlations between PLR, NLR, SII, and SIRI and atherosclerotic diseases. For instance, NLR has been found significantly associated with carotid plaque vulnerability,[34] intracranial artery stenosis and ischemic stroke,[35] the severity and recurrence of cerebral infarction in AIS patients,[11] and capable of predicting short-term mortality in AIS patients.[14] It has been reported that high PLR levels reflected more severe atherosclerosis and higher platelet activation,[36] and an elevated risk of plaque rupture, meanwhile increasing infarct volume and the incidence of poor outcomes in AIS patients.[15] Additionally, studies have shown a significant positive correlation between PLR and carotid artery stenosis.[37] SII was significantly associated with the risks of all-cause and cardiovascular mortality,[38] and it served as a predictor of stroke in middle-aged and elderly populations.[17] SIRI, similarly, was linked to all-cause and cardiovascular mortality risks[38] and was indicative of higher stroke severity and mortality.[18]

In summary, these studies indirectly suggested that PLR, NLR, SII, and SIRI might also be associated with ACI. In the present study, patients with ACI comprised 21.10% of the total study population, and PLR, NLR, SII, and SIRI were significantly higher in the ACI group compared to the non-ACI group. Based on these findings and the previous evidences, we hypothesized that these inflammatory markers might possess potential value in the screening for ACI in EH patients. To test this hypothesis, we conducted a comprehensive investigation of the relationship between ACI and the four inflammatory biomarkers in EH population by Spearman correlation analysis and multivariable logistic regression analysis. Additionally, we evaluated and compared the predictive abilities of each inflammatory marker for EH combined with ACI through ROC curve analysis. The results indicated that PLR, NLR, SII, and SIRI were independent risk factors for ACI in EH population, and each of them especially NLR demonstrated promising predictive value for ACI risk. To date, no previous reports have definitively indicated whether these inflammatory markers can aid in the screening of EH complicated with ACI. The current study filled this gap, providing convenient, economical, and effective adjunct tools for the screening of ACI in EH population. It is necessary in the future to validate these results in the context of large samples and multicenter studies, and to conduct further research on the pathogenesis of ACI in hypertensive patients influenced by these inflammatory markers.

In spite of the crucial clinical value provided by the present study, certain limitations could not be avoided, which may have implications for the generalizability of the finds. Firstly, patients lacking PLR, NLR, SII, and SIRI data were excluded. The exclusion criterion might limit the generalizability of the results, as a group of patients lacking these inflammatory markers due to various reasons (such as incomplete medical records or unavailable laboratory tests) could be considerable. Additionally, the current study was a cross-sectional observational analysis, which could not determine the temporal sequence between variables and thus restricted its capability to do deep exploration on the causal relationships. Furthermore, the limited sample size might influence the statistical accuracy of the results. A smaller size could lead to wider confidence intervals and reduce the ability to detect significant differences or associations, potentially resulting in Type II errors. Finally, some factors such as lipid-lowering medication doses, diabetes control, smoking, and comorbidities were not considered. These factors might influence the inflammatory markers and clinical outcomes studied, and their absence from the analysis might lead to bias.

Conclusion

Our findings indicated that EH patients complicated with ACI had a heavier inflammatory burden, as evidenced by elevated blood cell-derived biomarkers including PLR, NLR, SII and SIRI, compared to those without ACI. NLR, PLR, SII, and SIRI were found to have significant predictive value for the risk of ACI in EH population, with NLR showing the highest capability. Our results may provide a more cost-effective method to aid in the decision-making process regarding the necessity for further diagnostic imaging for ACI in EH population, thereby helping reduce the medical burden associated with previous blind screening. Additionally, these findings may offer clinical evidence and guidance for personalized and efficient treatment on EH patients complicated by ACI. Future studies are warranted to validate the stability and generalizability of our finding under the context of larger samples and multicenter settings and verify the role of leukocyte-based biomarkers in the occurrence, development and prognosis of EH complicated with ACI.

Data Sharing Statement

Data included in the present study may be accessible to the corresponding authors on reasonable requirements.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Helsinki Declaration (2013 revision) and received approval from the Ethics Committee of Henan Provincial People's Hospital (Approval No: MR-41-24-031650). A signed informed consent was obtained from each patient before participation. Notably, the research did not adversely affect the rights or health of the subjects, and stringent measures were implemented to protect the privacy and personal identity information of the participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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