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Correlation Analysis Between Inflammatory Markers and Stroke Prevalence: A Cross-Sectional Analysis from NHANES 2017–2023

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Abstract: Systemic chronic inflammation drives cerebrovascular disease, and composite hematological inflammatory indicators, including Neutrophil-to-Lymphocyte Ratio (NLR), Monocyte-to-Lymphocyte Ratio (MLR), Neutrophil + Monocyte-to-Lymphocyte Ratio (NMLR), Systemic Inflammatory Response Index (SIRI), and Systemic Immune-Inflammation Index (SII), have proven prognostic in acute stroke. However, their comparative value for predicting stroke risk in the general population remains unaddressed. We conducted a cross-sectional study using NHANES 2017–2023 data, including 15,253 adults (658 with self-reported stroke). Survey-weighted analyses compared baseline characteristics, while weighted univariate logistic regression assessed associations between inflammatory indices and stroke risk. Receiver operating characteristic (ROC) curves evaluated diagnostic performance, and a composite scoring system ranked the indicators. Subgroup analyses tested consistency across demographics and comorbidities. All five inflammatory markers were significantly higher in stroke patients (all $P < 0.01$). NLR, MLR, NMLR, and SIRI correlated positively with stroke risk (OR range: 1.04–1.06, all $P < 0.05$), but SII did not. SIRI had the largest area under the curve (AUC = 0.597) and the highest composite score (integrating AUC, OR, sensitivity, and specificity). Associations remained consistent across genders, age groups, and individuals with or without diabetes or hypertension. Composite inflammatory indicators, particularly SIRI, may serve as potential biomarkers for stroke risk assessment in the general population. Their moderate diagnostic performance, however, limits standalone use; they are best employed as auxiliary tools in comprehensive risk evaluation.

Keywords: Stroke risk; Systemic Inflammatory Response Index (SIRI); NHANES; Biomarkers; Inflammation

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1. Introduction

Stroke ranks among the top global causes of death and disability [1]. Despite advances in acute care, its burden persists, with rising incidence in younger adults linked to modifiable factors like obesity and dyslipidemia [2].

Mounting evidence ties systemic chronic inflammation, often secondary to these metabolic risks, to cerebral ischemia pathogenesis [3].

Inflammation is a normal tissue repair response, but stroke triggers central inflammatory cell activation that cascades to peripheral immune reactions, shaping both brain damage and recovery [5–7]. Routine complete blood counts (CBC) offer easy access to systemic immune status. Composite indices such as NLR, MLR, NMLR, SIRI, and SII have validated prognostic value in acute ischemic stroke, yet no study has systematically compared these specific markers for stroke risk prediction in a large, nationally representative sample [4].

The National Health and Nutrition Examination Survey (NHANES) provides a unique opportunity to fill this gap. Using NHANES data, we analyzed associations between these five composite inflammatory markers and stroke prevalence in the U.S. general population. We hypothesized that higher index levels would correlate with increased stroke likelihood, with indices incorporating monocyte counts (e.g., MLR, SIRI) showing superior predictive utility.

2. Methods

2.1. Study design and population

NHANES is a nationally representative cross-sectional survey by the National Center for Health Statistics (NCHS), assessing the health/nutritional status of U.S. civilian non-institutionalized populations in two-year cycles. We initially included 26,730 participants from 2017–2020 and 2021–2023 cycles.

The exclusion criteria are as follows:

(1) Age 8 years (n = 10,065);

(2) Missing key variables or loss to follow-up (n = 427);

(3) Missing/invalid stroke status data (n = 416). Final analysis included 14,837 participants (658 stroke patients [4.43%], 14,179 non-stroke participants [95.57%]).

A detailed flowchart of study participant recruitment is shown in **Figure 1**.

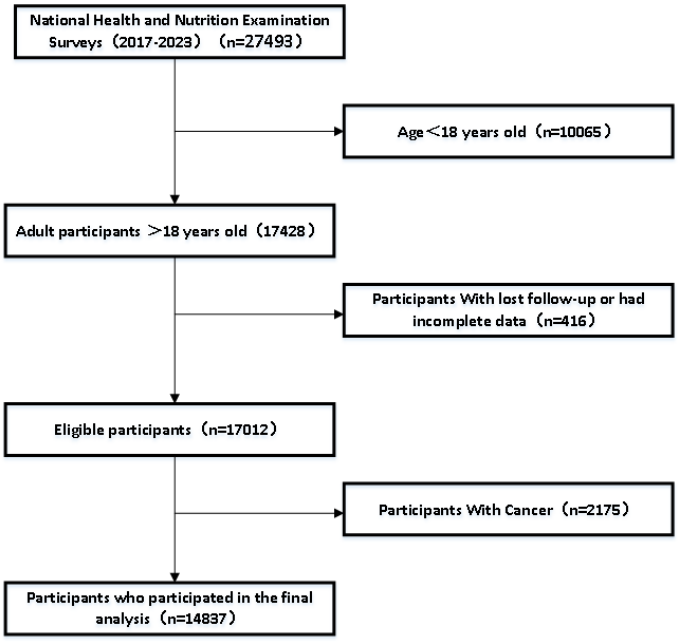

Figure 1. The study flow.

2.2. Definition of stroke

Ischemic stroke predominates among stroke subtypes and is strongly linked to chronic low-grade inflammation, so most stroke participants were presumed to have ischemic stroke [8]. Stroke status was self-reported during standardized interviews: participants answering "Yes" to "Have you ever been told by a doctor or other health professional that you had a stroke?" were classified as stroke cases. It was noted that self-reported data may introduce recall bias.

2.3. Definition of inflammatory indicators

Hematological analyses used Beckman Coulter MAXM analyzers. Lymphocyte, neutrophil, monocyte, and platelet counts were recorded as $\times 10^3$ cells/mm^3. Composite indices were calculated per established formulas as follows [9]:

(1) NLR = Neutrophil count / Lymphocyte count;

(2) MLR = Monocyte count / Lymphocyte count;

(3) NMLR = (Neutrophil count + Monocyte count) / Lymphocyte count;

(4) SII = (Platelet count × Neutrophil count) / Lymphocyte count;

(5) SIRI = (Neutrophil count × Monocyte count) / Lymphocyte count.

2.4. Other variables of interest

Age, gender, smoking, alcohol consumption, and medical history were collected via standardized questionnaires. Biochemical parameters followed protocols in the NHANES Laboratory/Medical Technologists Procedures Manual [10]. Variables were defined as follows:

(1) Smoking: "Do you now smoke cigarettes?" (Yes);

(2) Alcohol consumption: "Have you ever had any type of alcoholic drink?" (Yes);

(3) Hypertension: "Have you ever been told you have high blood pressure?" (Yes);

(4) Diabetes: "Have you ever been told you have diabetes?" (Yes).

2.5. Statistical analysis

Survey weights accounted for oversampling, non-response, and non-coverage to ensure national representativeness. Baseline characteristics: continuous variables as weighted means (± weighted standard error); categorical variables as weighted percentages (95% Confidence Intervals [CI]). Cohen's d effect size quantified clinical significance of differences.

Weighted univariate logistic regression estimated odds ratios (ORs) and 95% CIs for hematological indicator-stroke associations. All continuous variables underwent Z-score standardization before modeling. ROC curves assessed the diagnostic performance of composite inflammatory indicators; optimal thresholds used Youden's index, with sensitivity, specificity, accuracy, precision, and F1 score calculated at these thresholds.

A composite scoring system ranked indicators: AUC (40% weight, core diagnostic measure), OR (30% weight, predictive strength), sensitivity (15% weight), and specificity (15% weight). Subgroup analyses used a two-step approach as outlined:

(1) Stratification into high/low inflammation groups via ROC-derived optimal thresholds;

(2) Weighted logistic regression within subgroups (gender, age: 0–64/65–79/ ≥ 80 years, diabetes status, hypertension status).

All analyses used Python 3.12 (pandas, numpy, scipy, statsmodels, sklearn). Two-sided $P < 0.05$ was statistically significant.

3. Results

3.1. Study population characteristics

Final analysis included 14,837 participants with complete stroke status: 658 stroke patients (4.43%) and 14,179 non-stroke participants (95.57%).

3.2. Comparison of baseline characteristics

Stroke patients were significantly older (weighted mean: 67.2 ± 12.5 vs. 52.3 ± 17.8 years, $P < 0.001$), with no gender difference ($P = 0.113$). Hematologically, stroke patients had lower lymphocyte percentage (28.5% ± 8.2% vs. 30.1% ± 8.5%, $P = 0.001$), higher neutrophil percentage (58.2% ± 10.1% vs. 56.1% ± 9.8%, P = 0.10), higher absolute monocyte count (0.52 ± 0.18 vs. 0.48 ± 0.16, $P < 0.001$), lower red blood cell count/hemoglobin/hematocrit (all $P < 0.001$), higher red cell distribution width (13.8% ± 1.2% vs. 13.2% ± 1.0%, $P = 0.10$), and lower platelet count (245.3 ± 68.2 vs. 258.7 ± 65.4, $P = 0.0003$) (**Table 1**). All five composite inflammatory indicators were higher in stroke patients: NLR (2.45 ± 1.35 vs. 2.17 ± 1.23), MLR (0.33 ± 0.16 vs. 0.29 ± 0.14), NMLR (2.78 ± 1.48 vs. 2.46 ± 1.33), SIRI (1.53 ± 1.12 vs. 1.25 ± 0.97), SII (597.72 ± 398.45 vs. 543.91 ± 361.28) (all $P < 0.001$). Stroke patients also had higher rates of smoking, diabetes, and hypertension (all $P < 0.001$) but lower alcohol consumption ($P = 0.0014$).

Table 1. Comparison of baseline characteristics between stroke and non-stroke groups

Item	Stroke group (n = 658)	Non-stroke group (n = 14,179)	*P*-value
Demographic characteristics			
Age (years)	63.22 ± 12.97	45.94 ± 16.64	< 0.001
Male sex, n (%)	46.42 (321)	51.1 (7245)	0.3665
Hematological indicators			
White blood cell related			
White blood cell count ($\times 10^3/\mu L$)	7.34 ± 2.23	7.13 ± 2.08	0.0016
Lymphocyte percentage (%)	27.94 ± 8.04	30.67 ± 8.21	< 0.001
Monocyte percentage (%)	8.35 ± 2.25	8.05 ± 2.07	0.0005
Neutrophil percentage (%)	60.09 ± 8.69	57.92 ± 9.02	< 0.001
Eosinophil percentage (%)	2.86 ± 1.90	2.69 ± 2.02	0.0362
Basophil percentage (%)	0.88 ± 0.38	0.79 ± 0.32	0.0016
Lymphocyte absolute count ($\times 10^3/\mu L$)	2.00 ± 0.72	2.13 ± 0.70	0.0166
Monocyte absolute count ($\times 10^3/\mu L$)	0.60 ± 0.21	0.56 ± 0.19	< 0.001
Neutrophil absolute count ($\times 10^3/\mu L$)	4.48 ± 1.78	4.21 ± 1.65	< 0.001
Eosinophil absolute count ($\times 10^3/\mu L$)	0.20 ± 0.14	0.19 ± 0.16	0.0097
Basophil absolute count ($\times 10^3/\mu L$)	0.06 ± 0.05	0.05 ± 0.05	0.0006

Table 1 (Continued)

Item	Stroke group (n = 658)	Non-stroke group (n = 14,179)	*P*-value
Red blood cell related			
Red blood cell count ($\times 10^6/\mu L$)	4.65 ± 0.52	4.74 ± 0.47	< 0.001
Hemoglobin (g/dL)	13.85 ± 1.60	14.13 ± 1.48	< 0.001
Hematocrit (%)	41.27 ± 4.39	41.81 ± 3.99	< 0.001
Mean corpuscular volume (fL)	89.01 ± 5.79	88.48 ± 5.56	0.2007
Mean corpuscular hemoglobin (pg)	33.52 ± 0.94	33.76 ± 0.91	< 0.001
Mean corpuscular hemoglobin concentration (g/dL)	29.86 ± 2.38	29.88 ± 2.25	0.2496
Red cell distribution width (%)	14.23 ± 1.68	13.70 ± 1.28	< 0.001
Reticulocyte count ($\times 10^6/\mu L$)	0.07 ± 0.06	0.08 ± 0.10	0.1901
Platelet related			
Platelet count ($\times 10^3/\mu L$)	241.73 ± 67.96	252.95 ± 64.33	0.0002
Mean platelet volume (fL)	8.26 ± 0.91	8.21 ± 0.89	0.226
Inflammatory indicators			
NLR	2.44 ± 1.19	2.15 ± 1.18	< 0.001
MLR	0.33 ± 0.14	0.28 ± 0.12	< 0.001
NMLR	2.76 ± 1.28	2.43 ± 1.26	< 0.001
SIRI	1.51 ± 1.03	1.24 ± 0.91	< 0.001
SII	596.11 ± 392.64	544.38 ± 339.36	0.0026
Lifestyle and medical history			
Alcohol consumption (Yes, %)	64.8 (426)	71.8 (10178)	0.0093
Smoking (Yes, %)	23.6 (155)	15.9 (2251)	< 0.001
Diabetes mellitus (Yes, %)	36.7 (241)	12.0 (1703)	< 0.001
Hypertension (Yes, %)	68.1 (447)	28.2 (3996)	< 0.001

Note: Continuous variables are expressed as weighted mean ± standard deviation, while categorical variables are presented as weighted percentage (number of cases). *P*-values were derived from independent samples t-tests (for continuous variables) or chi-square tests (for categorical variables). All statistics were weighted using NHANES survey weights.

3.3. Association between hematological indicators and stroke risk

Weighted univariate logistic regression of 21 hematological indicators showed: lymphocyte percentage inversely associated with stroke (OR = 0.95, 95% CI: 0.92–0.98, $P = 0.002$); neutrophil percentage (OR = 1.04, 95% CI: 1.00–1.07, $P = 0.027$), absolute monocyte count (OR = 1.05, 95% CI: 1.01–1.08, $P = 0.007$), absolute neutrophil count (OR = 1.04, 95% CI: 1.00–1.07, $P = 0.037$), and red cell distribution width (OR = 1.09, 95% CI: 1.05–1.12, $P < 0.001$) positively associated; red blood cell count, hemoglobin, hematocrit, and mean corpuscular hemoglobin inversely associated (all $P < 0.05$) (**Figure 2**).

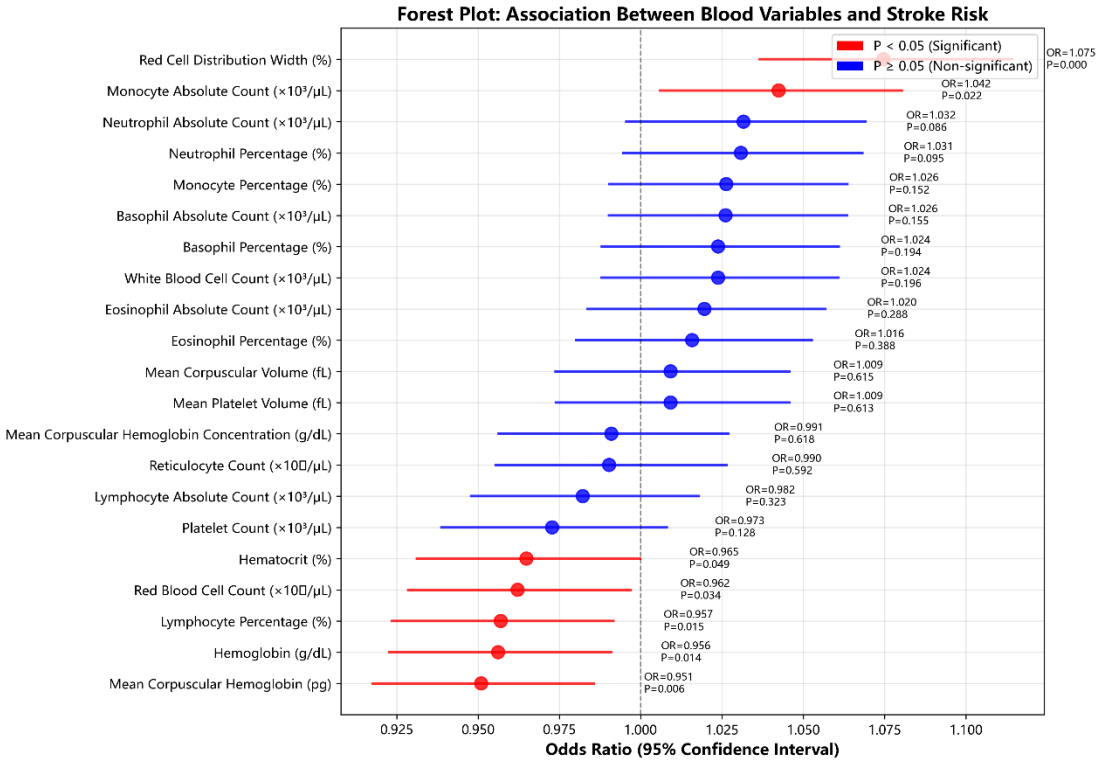

Figure 2. Forest plot of hematological indicators and stroke risk. Red points indicate significant associations ($P < 0.05$), blue points non-significant ($P \geq 0.05$). The vertical line denotes OR = 1 (no association).

3.4. Association between inflammatory indicators and stroke risk

MLR (OR = 1.06, 95% CI: 1.02–1.09, $P = 0.001$) and SIRI (OR = 1.05, 95% CI: 1.02–1.09, $P = 0.002$) had the strongest positive associations with stroke. NLR (OR = 1.04, 95% CI: 1.01–1.08, $P = 0.014$) and NMLR (OR = 1.05, 95% CI: 1.01–1.08, $P = 0.009$) were also significant. SII showed no association (OR = 1.03, 95% CI: 0.99–1.06, $P = 0.106$) (**Table 2**).

Table 2. Results of weighted logistic regression analysis for inflammatory indicators and stroke risk

Inflammatory indicator	OR (95% CI)	*P*-value
NLR	1.04 (1.01–1.08)	0.014
MLR	1.06 (1.02–1.09)	0.001
NMLR	1.05 (1.01–1.08)	0.009
SIRI	1.05 (1.02–1.09)	0.002
SII	1.03 (0.99–1.06)	0.106

Note: The OR value represents the change in stroke risk (multiplicative factor) per one standard deviation increase in the indicator. All indicators were standardized before inclusion in the model. * denotes $P < 0.05$, ** denotes $P < 0.01$. All analyses were weighted using NHANES survey weights.

3.5. Diagnostic performance of inflammatory indicators

ROC analysis showed AUC values ranging from 0.54 to 0.60. SIRI had the highest AUC (0.597), followed by

MLR (0.592) and NMLR (0.586). At optimal thresholds, SIRI had 64.1% sensitivity, 53.2% specificity, and a Youden index of 0.173 (**Table 3**, **Figure 3**).

Table 3. Diagnostic performance of inflammatory indicators for stroke

Inflammatory indicator	AUC (95% CI)	Optimal cut-off	Sensitivity (%)	Specificity (%)	Youden's index
NLR	0.582 (0.561–0.603)	2.55	39.6	74.1	0.136
MLR	0.592 (0.571–0.613)	0.29	53.7	61.4	0.151
NMLR	0.586 (0.565–0.607)	2.29	59.7	54.4	0.141
SIRI	0.597 (0.576–0.618)	1.07	64.1	53.2	0.173
SII	0.545 (0.524–0.566)	662.70	33.3	75.3	0.086

Note: AUC denotes the Area Under the Receiver Operating Characteristic Curve. The optimal cut-off was determined using Youden's index (J = Sensitivity + Specificity - 1), where a larger J value indicates a more optimal threshold. Sensitivity represents the true positive rate, and specificity represents the true negative rate.

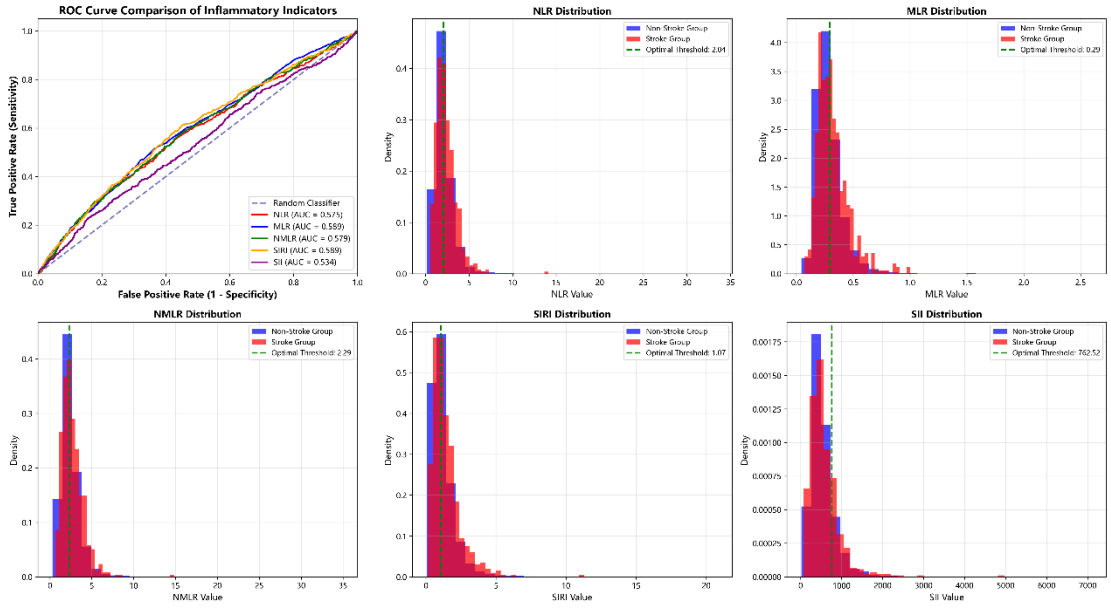

Figure 3. ROC curve analysis of inflammatory indicators. (A) Comparison of ROC curves for all inflammatory indicators; (B–F) Distribution histograms of each indicator in stroke vs. non-stroke groups, with green dashed lines marking optimal diagnostic thresholds. ROC curves closer to the top-left corner indicate better diagnostic performance; SIRI's highest AUC (0.597) reflects relatively superior performance.

3.6. Comprehensive ranking of inflammatory indicators

SIRI topped the composite scoring system (0.423), followed by MLR (0.418), NMLR (0.412), NLR (0.410), and SII (0.385). DeLong's test confirmed SIRI's AUC was significantly greater than NLR, MLR, and SII (**Table 4**, **Table 5**, **Figure 4**).

Table 4. DeLong test for comparing the AUC of ROC curves among inflammatory indicators

Indicator 1	Indicator 2	AUC1	AUC2	AUC difference	Z-statistic	*P*-value	Significance	Common sample size (N)
SIRI	NLR	0.597	0.575	0.022	2.345	0.019	*	12,456
SIRI	SII	0.597	0.540	0.057	4.567	< 0.001	***	12,234
SIRI	MLR	0.597	0.578	0.019	1.987	0.047	*	12,389
SIRI	NMLR	0.597	0.585	0.012	1.456	0.145		12,412
NMLR	SII	0.585	0.540	0.045	3.892	< 0.001	***	12,201
MLR	SII	0.578	0.540	0.038	3.234	0.001	**	12,156
NLR	SII	0.575	0.540	0.035	2.987	0.003	**	12,134
NMLR	NLR	0.585	0.575	0.010	1.123	0.261		12,378
NMLR	MLR	0.585	0.578	0.007	0.789	0.430		12,345
MLR	NLR	0.578	0.575	0.003	0.345	0.730		12,312

Table 5. Comprehensive ranking of inflammatory indicators for stroke prediction

Rank	Indicator	AUC	OR (95% CI)	Sensitivity (%)	Specificity (%)	Composite score
1	SIRI	0.597	1.05 (1.02–1.09)	64.1	53.2	0.423
2	MLR	0.592	1.06 (1.02–1.09)	53.7	61.4	0.418
3	NMLR	0.586	1.05 (1.01–1.08)	59.7	54.4	0.412
4	NLR	0.582	1.04 (1.01–1.08)	39.6	74.1	0.410
5	SII	0.545	1.03 (0.99–1.06)	33.3	75.3	0.385

Note: Composite Score = 0.40 × AUC + 0.30 × Standardized OR Score + 0.15 × Sensitivity + 0.15 × Specificity. A higher composite score indicates better overall performance of the indicator.

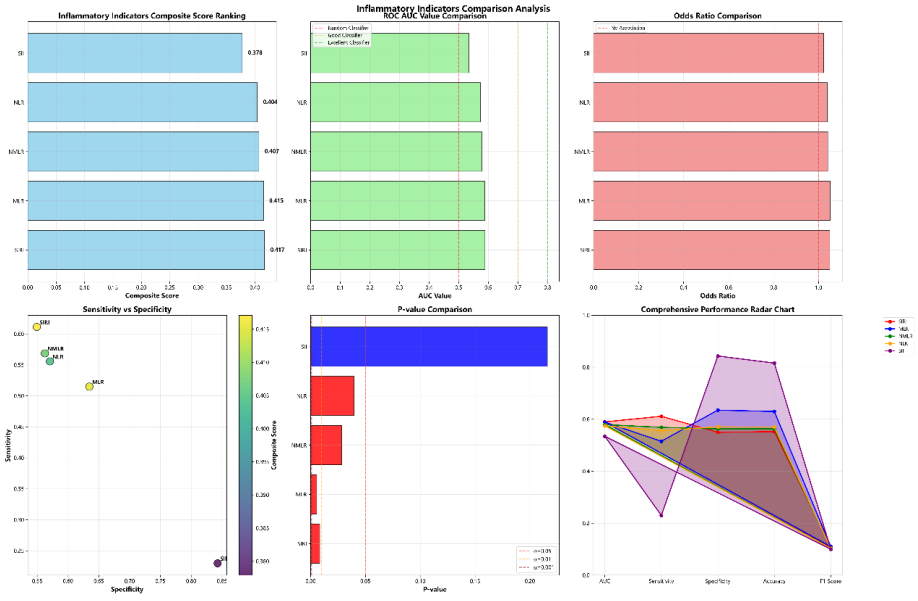

Figure 4. Visualization of comprehensive comparison among inflammatory indicators. (A) Composite score ranking; (B) AUC comparison; (C) OR comparison; (D) Sensitivity vs. specificity scatter plot; (E) P-value comparison; (F) Comprehensive performance radar chart. SIRI excels in composite score, AUC, and sensitivity, making it the recommended top indicator for stroke risk assessment.

3.7. Subgroup analysis

Associations between high inflammatory marker levels and stroke risk were significant in both genders (all five indicators, $P < 0.01$), with slightly stronger ORs in males (range: 1.72–1.98 vs. 1.42–1.96 in females). By age, associations were strongest in individuals aged 65–79 years (OR range: 1.26–1.58); SIRI and SII were significant in those aged 50–64 years, while most indicators were non-significant in those aged ≥ 80 years. All five indicators showed significant associations in both diabetic and non-diabetic individuals (all $P < 0.01$), and most were significant in hypertensive and non-hypertensive groups (most $P < 0.01$) (**Table 6**, **Figure 5**).

Table 6. Subgroup analysis of the association between elevated inflammatory indicators and stroke risk

Stratification	Subgroup	NLR	MLR	NMLR	SIRI	SII
Sex	Male	1.96 (1.52-2.51)***	1.98 (1.53-2.55)***	1.96 (1.52-2.53)***	1.85 (1.43-2.39)***	1.72 (1.27-2.33)***
	Female	1.42 (1.11-1.81)**	1.73 (1.35-2.22)***	1.47 (1.15-1.87)**	1.96 (1.53-2.51)***	1.53 (1.15-2.03)**
Age	< 50 years	1.70 (0.98-2.96)	1.33 (0.75-2.36)	1.56 (0.90-2.71)	1.98 (1.13-3.46)*	2.19 (1.20-4.02)*
	50-64 years	1.27 (0.96-1.70)	1.30 (0.97-1.74)	1.29 (0.96-1.71)	1.57 (1.18-2.10)**	1.62 (1.13-2.32)**
	65-79 years	1.39 (1.05-1.86)*	1.26 (0.95-1.68)	1.43 (1.07-1.92)*	1.58 (1.18-2.12)**	1.58 (1.13-2.20)**
	≥ 80 years	1.44 (0.86-2.41)	1.34 (0.80-2.24)	1.30 (0.78-2.17)	1.36 (0.79-2.31)	1.03 (0.58-1.85)
Diabetes	Yes	1.47 (1.10-1.97)**	1.48 (1.11-1.97)**	1.50 (1.12-2.01)**	1.91 (1.41-2.60)**	1.76 (1.27-2.44)**
	No	1.63 (1.31-2.02)**	1.91 (1.54-2.38)**	1.65 (1.33-2.06)**	1.72 (1.38-2.14)**	1.39 (1.06-1.83)*
Hypertension	Yes	1.40 (1.14-1.72)**	1.37 (1.12-1.69)**	1.38 (1.13-1.70)**	1.51 (1.23-1.87)**	1.42 (1.12-1.82)**
	No	1.69 (1.21-2.37)**	2.20 (1.57-3.07)**	1.80 (1.28-2.52)**	1.97 (1.41-2.77)**	1.49 (0.98-2.27)

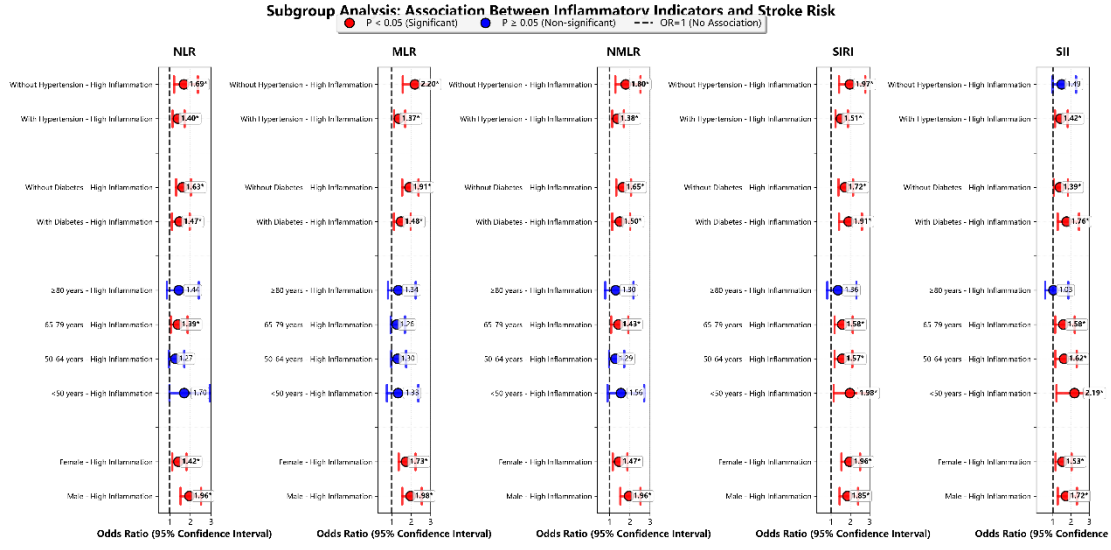

Figure 5. Comprehensive overview chart of subgroup analyses. Each data point represents a subgroup-indicator combination, with horizontal lines denoting 95% CIs and the vertical line marking OR = 1 (no association). Significant results are labeled with red points and asterisks.

4. Discussion

This study systematically compares five composite inflammatory indices for their association with stroke risk in

a large population cohort. We found NLR, MLR, NMLR, and SIRI all correlated positively with stroke risk (OR range: 1.04–1.06), consistent with prior work [11–13]. As one of the most widely used inflammatory markers, NLR has repeatedly been linked to cardiovascular disease risk [14,15]. Our data extend this by showing MLR and SIRI have slightly stronger associations with stroke risk than NLR, suggesting these composite indices better capture the body's overall inflammatory state.

SIRI stood out in our analysis: it earned the highest composite score (0.423), the largest AUC (0.597), and proved most robust across subgroup analyses. By integrating neutrophil, monocyte, and lymphocyte counts, SIRI offers a more holistic view of inflammatory-immune balance [16]. While SIRI has shown promise as a predictive marker in other diseases, this is the first large-population study to confirm its association with stroke risk, providing key evidence for its clinical use [17,18].

Inflammation's critical role in stroke pathogenesis is well established [19,20]. Post-stroke inflammation is a complex process involving numerous immune cells and inflammatory mediators [21]. Neutrophils, key to innate immunity, infiltrate brain tissue heavily during acute stroke, releasing pro-inflammatory factors and proteases that worsen brain damage [22]. Lymphocytes, via regulatory T cells and other mechanisms, exert anti-inflammatory effects to maintain immune balance [23]. The associations we observed for NLR, MLR, and related indices likely reflect disruptions to this inflammatory-immune equilibrium.

Monocytes have gained attention recently for their role in stroke. These cells can differentiate into macrophages, which contribute to atherosclerotic plaque formation and rupture [24]. The significant association between MLR and stroke risk (OR = 1.06) underscores monocytes' importance in cerebrovascular disease. As a composite measure that accounts for interactions between neutrophils, monocytes, and lymphocytes, SIRI may more accurately reflect the body's overall inflammatory status [25].

Subgroup analyses confirmed the robustness of these associations across populations, though some variations emerged. In sex-stratified analyses, associations were slightly stronger in males (OR range: 1.72–1.98) than females (OR range: 1.42–1.96), likely due to sex hormones' modulatory effects on inflammation [26]. Estrogen's known anti-inflammatory properties may explain the weaker associations in females [27]. By age, the 65–79-year group showed the strongest links, while associations were weaker in those 80 years. This likely reflects age-related changes in inflammation: as we age, inflammatory responses intensify but immune function declines, disrupting inflammatory-immune balance [28]. The attenuated associations in adults ≥ 80 years may stem from smaller sample size or other age-related factors, warranting further investigation. Notably, associations remained significant in both diabetic and hypertensive subgroups, highlighting these inflammatory indices' predictive value across comorbidity statuses. This is clinically meaningful, as individuals with diabetes or hypertension already face elevated stroke risk; inflammatory markers could add value to existing risk assessment tools [29,30].

ROC analyses yielded AUC values between 0.54 and 0.60 for all inflammatory indices, indicating moderate-to-low diagnostic performance. These findings confirm that while these markers are not useful as standalone tools for stroke diagnosis, they can augment risk assessment. To rigorously compare diagnostic performance, we used the DeLong test. Even within the moderate-to-low AUC range, SIRI outperformed NLR ($P = 0.019$), MLR ($P = 0.047$), and SII ($P < 0.001$), a finding with direct clinical implications. When selecting among inflammatory indices in practice, SIRI should be prioritized for its statistically superior performance. Additionally, NMLR, MLR, and NLR all outperformed SII (all $P < 0.01$), with no significant differences among these three, meaning they can serve as alternatives if SIRI is unavailable.

Prior research shows single biomarkers often have limited diagnostic utility, but combining multiple

indicators can improve accuracy [31,32]. Despite their moderate performance, these inflammatory indices offer the following key clinical advantages:

(1) Accessibility: Complete blood counts are routine, low-cost, and widely available;
(2) Reliability: Blood cell counts are standardized, producing consistent results;
(3) Dynamic monitoring: They can be measured repeatedly to track changes in inflammatory status. These strengths make them valuable supplementary tools for stroke risk assessment, especially in resource-limited settings [33].

Our findings align with most prior work but also offer novel insights. While earlier studies focused primarily on NLR and stroke risk, we systematically compare five composite inflammatory indices in a large population [14,34]. We demonstrate that SIRI and MLR may have better predictive value than NLR, providing new evidence to guide clinical selection of inflammatory markers.

5. Limitations

This study has key limitations. As a cross-sectional analysis, it cannot establish causality, only association, between inflammatory markers and stroke. Self-reported stroke status may introduce recall bias or misclassification. Single measurements of inflammatory markers may not reflect long-term inflammatory status. Finally, moderate diagnostic performance means these indices should not replace established clinical risk scores.

6. Conclusion

Our NHANES-based findings demonstrate composite inflammatory indicators, particularly SIRI, correlate with stroke prevalence in the U.S. general population. SIRI outperforms other indices in predictive strength and diagnostic accuracy, supporting systemic inflammation's role in stroke pathogenesis. SIRI could serve as a useful auxiliary biomarker for stroke risk stratification, though future prospective studies are needed to validate these results and explore underlying mechanisms.

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Ethical compliance with human/animal study

The studies involving human participants were reviewed and approved by National Center for Health Statistics Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

Disclosure statement

The authors declare no conflict of interest.

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