Neurology Asia 2026; 31(2) : 427 – 437

Associations between hematological inflammatory markers, infarct volume, and stroke severity in patients with obstructive sleep apnea and anterior circulation non-large artery occlusion

[1,2]Li Zhang *MD*, [1,2]Jun-Qiang Bao *BMed*, [1,2]Yan-Ying Zhao *MD*, [3]Di Wu *MD*, [1,2]Xiao-Yun Liu *MD*

[1]Department of Neurology, The First Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China; [2]Department of Neurology, Hebei Hospital of Xuanwu Hospital Capital Medical University, Shijiazhuang, Hebei Province, China; [3]Department of Neurology and China-America Institute of Neuroscience, Xuanwu Hospital, Capital Medical University, Beijing, China.

Abstract

Background: Neuroinflammatory processes are recognized as critical contributors to the pathophysiology of acute ischemic stroke (AIS). Hematological inflammatory markers have demonstrated a strong association with the progression and clinical prognosis of AIS. *Methods:* A retrospective review was conducted on the clinical records of patients with AIS involving the anterior circulation without evidence of large artery occlusion (LAO) who received treatment at a single institution between January 2019 and September 2021. Participants were stratified according to the presence or absence of obstructive sleep apnea (OSA) prior to stroke onset. Multiple linear regression models were applied to evaluate the relationships among hematological inflammatory markers, vascular risk factors, infarct volume, and stroke severity. *Results:* Infarct volume demonstrated a significantly positive association with both the systemic immune-inflammation index (SII) ($p = 0.002$) and mean platelet volume (MPV) ($p = 0.03$). Stroke severity at the time of hospital admission demonstrated a significant negative association with pre-stroke OSA history ($p = 0.026$) and the monocyte-to-lymphocyte ratio (MLR) ($p = 0.002$), and a significant positive association with neutrophil count ($p < 0.001$) and platelet distribution width (PDW) ($p = 0.048$). No statistically significant relationship was identified between the SII and stroke severity, or between a history of pre-stroke OSA and infarct volume.
Conclusion: Elevated levels of SII and MPV may be independently associated with increased infarct volume in patients with AIS. However, our findings did not reveal an association between pre-stroke OSA with increased infarct volume or greater stroke severity at presentation.

Keywords: Acute ischemic stroke, infarct volume, inflammatory markers, obstructive sleep apnea, stroke severity, systemic immune-inflammation index

INTRODUCTION

Stroke remains the leading cause of mortality in China and the second most common cause of death globally, contributing to considerable disability, societal burden, and elevated healthcare costs.[1] In recent years, neuroinflammation has emerged as a key area of focus in stroke research. Acute ischemic stroke (AIS) initiates both intravascular and peripheral inflammatory responses. Evidence from multiple studies has indicated that the inflammatory cascade is rapidly activated following vascular occlusion, thereby aggravating neuronal injury and contributing to neurological impairment.[2,3] The complete blood count (CBC) represents a cost-effective and routinely utilized diagnostic modality in clinical settings. Inflammatory responses are mediated by various hematologic

Address correspondence to: Xiao-Yun Liu, Department of Neurology, The First Hospital of Hebei Medical University, No.89 of Donggang Road, Yuhua District, Shijiazhuang 050031, Hebei Province, China. E-mail: audrey-l@163.com; Di Wu, Department of Neurology and China-America Institute of Neuroscience, Xuanwu Hospital, Capital Medical University, No. 45 of Changchun Street, Beijing 100053, China. E-mail: seadi-wu@163.com

Date of Submission: 5 September 2025; Date of Acceptance: 31 January 2026

https://doi.org/10.54029/2026inn

components, including white blood cells, neutrophils, lymphocytes, monocytes, and platelets.[4] Composite hematological indices such as the systemic immune-inflammation index (SII), calculated as neutrophil count × platelet count / lymphocyte count, have been investigated in several studies.[5,6] These indices are considered reliable indicators of systemic inflammation and have been closely associated with the pathogenesis and prognosis of cerebrovascular disorders.

Obstructive sleep apnea (OSA), the most prevalent form of sleep apnea, is characterized by recurrent upper airway obstruction during sleep. Obstructive sleep apnea (OSA) and habitual snoring have been identified as independent risk factors for conditions such as hypertension, arrhythmias, coronary artery disease, myocardial infarction, and ischemic stroke.[7,8] OSA has been reported to affect functional recovery after stroke and to worsen prognosis by amplifying cardiovascular risk factors commonly linked with stroke.[9] Nevertheless, findings from a prospective longitudinal study indicated no significant association between OSA and stroke after adjusting for age, sex, and body mass index (BMI), rendering the impact of OSA on stroke outcomes inconclusive.[10]

Currently, there is a paucity of research examining the relationship between hematological inflammatory markers and AIS in patients with OSA. Additionally, the presence of LAO may substantially influence infarct size and prognosis, thereby confounding analysis that include such cases. To address these gaps, the present retrospective study was designed to explore the associations between hematological markers, infarct volume, and stroke severity in patients with OSA and AIS involving the anterior circulation in the absence of culprit LAO. These findings may offer additional insights into AIS pathogenesis and inform strategies for its prevention and clinical management.

METHODS

Study design and participants

This retrospective observational study included adult patients aged 18 years or older who experienced a first-ever episode of AIS and were consecutively admitted to the Department of Neurology at Xuanwu Hospital between January 2019 and September 2021. Eligibility criteria required presentation within 72 hours of symptom onset and completion of cranial magnetic resonance imaging (MRI) within 7 days of onset. Patients were divided into OSA and non-OSA groups. The OSA group included patients who had been diagnosed with OSA prior to AIS and had an apnea-hypopnea index (AHI) ≥15 but had not received OSA treatment. The non-OSA group included patients who did not snore or only snored occasionally (1–2 nights per week) before AIS onset and were assessed to be at low risk for OSA according to the Berlin questionnaire and STOP-Bang questionnaire. To reduce potential confounding from prior cerebrovascular events that may influence sleep characteristics or inflammatory responses, patients with a history of stroke were excluded. Additional exclusion criteria included infarction involving the posterior circulation or culprit large artery occlusion (LAO) in the anterior circulation, specifically involving the internal carotid artery, middle cerebral artery, or anterior cerebral artery. Patients were also excluded if neurological deficits resolved within 1 hour of onset and MRI revealed no evidence of AIS lesions. Further exclusion criteria were as follows: 1) Intracranial hemorrhage, brain tumors, demyelinating diseases, inflammatory conditions of the central nervous system, history of craniotomy or severe head trauma, idiopathic intracranial hypertension, aneurysms, or arteriovenous fistulas; 2) Baseline oxygen saturation <90%, presence of tracheostomy, ongoing mechanical ventilation, or receipt of other therapeutic positive airway pressure interventions; 3) Acute or chronic pulmonary conditions (e.g., chronic obstructive pulmonary disease, bronchitis, interstitial pneumonia, pulmonary infections), acute myocardial infarction, other severe cardiopulmonary dysfunction, malignant tumors, or hypothyroidism; 4) Recent surgery involving the upper airway; 5) Neuromuscular junction disorders such as myasthenia gravis; 6) Neurodegenerative conditions including Parkinson's disease, spinocerebellar degeneration, Alzheimer's disease, or motor neuron disease; 7) Other sleep disorders such as insomnia or restless legs syndrome; 8) Pregnancy; 9) Presence of chronic intracranial lesions on initial T2-weighted imaging; 10) Incomplete clinical or imaging data; 11) Absence of informed consent; and 12) Modified Rankin Scale (mRS) score ≥1 prior to AIS onset. The study protocol received approval from the Institutional Ethics Committee of Xuanwu Hospital, and written informed consent was

obtained from all participants or their legal guardians prior to enrollment.

Data collection of study participants

All participants received treatment in accordance with the *Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke (2018)* during the acute phase of AIS.

Baseline demographic data were recorded along with detailed histories of vascular risk factors, including hypertension, diabetes mellitus, coronary artery disease, hyperlipidemia, atrial fibrillation, transient ischemic attack (TIA), hyperuricemia, hyperhomocysteinemia, alcohol consumption, and tobacco use. Additionally, vital signs and various diagnostic and laboratory parameters obtained during hospitalization were documented. These included CBC, blood glucose levels, liver and renal function tests, lipid profiles, electrolytes, myocardial enzymes, coagulation parameters, electrocardiograms, carotid ultrasound, transcranial Doppler (TCD), computed tomography angiography (CTA) or magnetic resonance angiography (MRA), digital subtraction angiography (DSA), 24-hour Holter monitoring, two-dimensional echocardiography, and chest radiography or CT. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

Clinical assessment of AIS

Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). The etiology of AIS was determined according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, which categorizes ischemic stroke into five subtypes:[11] large-artery atherosclerosis, cardioembolism, small-vessel occlusion, stroke of other determined etiologies, and stroke of undetermined etiology. Each participant's stroke subtype was documented accordingly.

Clinical assessment of OSA

The AHI threshold of ≥15 was selected based on epidemiological evidence indicating increased cardiovascular risk in individuals with moderate to severe OSA.[12] Previous large-scale population-based studies demonstrated an approximately threefold increase in stroke risk associated with AHI ≥15.[13,14]

The patients in the non-OSA group were assessed as being at low-risk for OSA based on the Berlin Questionnaire and the STOP-Bang Questionnaire.[15,16] The Berlin Questionnaire comprises 10 questions and includes height and weight measurements, grouped into three categories: snoring and breathing cessation (Category 1, Items 1–5), symptoms of excessive daytime sleepiness (Category 2, Items 6–9), and BMI and hypertension (Category 3, Item 10). Participants with no positive scores or positive scores only in Category 1 were classified as low-risk for OSA.[15] The STOP-Bang Questionnaire includes the four questions from the STOP questionnaire along with four demographic items (snoring, fatigue, observed apneas, hypertension, BMI, age, neck circumference, and male sex), yielding a total of eight binary questions. A total score between 0 and 2 indicated low OSA risk.[17,18] For participants who did not complete the questionnaires during hospitalization or follow-up visits, sleep history was obtained through clinical records and telephone interviews conducted with spouses. Patients were excluded from the analysis if family members could not provide sufficient information regarding the patient's sleep behavior.

Other measurements

All cranial MRI scans were independently assessed by two experienced neuroradiologists. Discrepancies were resolved through consensus. AIS lesions were identified using diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences. The number, anatomical distribution of lesions (cortical, subcortical, or deep white matter), and the corresponding vascular territories were recorded. The volume of each infarct was calculated using three orthogonal dimensions: the maximum diameter (A), its perpendicular (B), and the cumulative thickness across all slices where the lesion appeared (C). Lesion volume was calculated using the formula $A \times B \times C / 2$ and expressed in milliliters, following the methodology outlined in the International Carotid Stenting Study (ICSS)-MRI substudy.[19] Total infarct volume was defined as the cumulative volume of all infarcted regions. Lesion measurements were independently conducted by two blinded observers to ensure objectivity.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). Quantitative data following a normal

distribution were reported as mean ± standard deviation, while non-normally distributed quantitative data were presented as median and interquartile range (IQR). Categorical variables were expressed as percentages. Group comparisons of quantitative data were performed using the independent samples *t*-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical data were analyzed using the chi-square test to evaluate differences between the OSA and non-OSA groups.

Multiple linear regression analysis was used to assess the associations between infarct volume, neurological impairment, OSA status, hematological markers, and additional risk factors associated with cerebrovascular disease. Dependent variables in the regression analysis model included infarct volume and NIHSS score at admission. Independent variables encompassed demographic and clinical factors such as hematological markers (red blood cell count, hematocrit, white blood cell count, lymphocyte count, eosinophil count, platelet count, mean platelet volume [MPV], platelet distribution width, red cell distribution width, neutrophil count, monocyte count, neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR], monocyte-to-lymphocyte ratio [MLR], monocyte-to-high-density lipoprotein ratio [MHR], systemic immune-inflammation index [SII, neutrophil count × platelet count / lymphocyte count], systemic coagulation-inflammation index [SCI, platelet count × fibrinogen / white blood cell count], and systemic inflammatory response index [SIRI, neutrophil count × monocyte count / lymphocyte count]. Other included covariates were sex, age, BMI, hypertension, diabetes mellitus, TIA, hyperlipidemia, coronary artery disease, atrial fibrillation, hyperuricemia, OSA status (OSA or non-OSA group), hyperhomocysteinemia, smoking status, alcohol consumption, thrombolytic therapy, albumin level, D-dimer, and plasma fibrinogen concentration. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

Overall baseline data

A total of 89 patients with AIS met the inclusion criteria for this study. Among them, 33 were assigned to the OSA group and 56 to the non-OSA group. The overall prevalence of OSA (AHI ≥ 15) was 37.08% (30 males and 3 females). Within the OSA group, 23 participants had complete polysomnographic records with documented AHI values ranging from 16.10 to 64.20 (median: 36.70). The remaining participants had a confirmed diagnosis of OSA with AHI ≥ 15, although specific polysomnographic data were not available. Baseline peripheral oxygen saturation (SpO_2) ranged from 87% to 97% (median: 93.6%), and the minimum SpO_2 ranged from 30% to 84% (median: 75%). Demographic and baseline clinical characteristics are presented in Table 1. The overall age range of the cohort was 30 to 86 years (mean: 58.28 years), with males comprising 77.53% of the total sample.

A significantly higher proportion of male participants was observed in the OSA group compared to the non-OSA group (90.91% vs. 69.64%; p = 0.02). Additionally, BMI was significantly higher in the OSA group (26.20 vs. 24.22 kg/m²; p = 0.001). The prevalence of diabetes mellitus was also significantly greater in the OSA group (57.56% vs. 28.57%; p = 0.007). Furthermore, patients in the OSA group demonstrated significantly elevated levels of white blood cells (p = 0.011), neutrophils (p = 0.034), monocytes (p = 0.008), MHR (p = 0.026), and fibrinogen (p = 0.006) compared to the non-OSA group.

Differences in infarct volume and NIHSS scores between groups

DWI revealed no statistically significant difference in infarct volume between the OSA and non-OSA groups (median: 2.96 mL [IQR: 12.57]; non-OSA: 5.22 mL [IQR: 19.65], respectively, p = 0.262). Additionally, there was no significant difference in NIHSS scores at admission between the OSA and non-OSA groups, with both groups exhibiting a median score of 4 (p = 0.527) (Table 2).

Multiple linear regression analysis

Infarct volume demonstrated a significant positive association with SII (p = 0.002; 95% confidence interval [CI], 0.000 to 0.001) and MPV (p = 0.03; 95% CI, 0.013 to 0.251). NIHSS score at admission demonstrated a significant negative association with MLR (p = 0.002; 95% CI, -3.297 to -0.758) and a history of OSA (p = 0.026; 95% CI, -0.734 to -0.048), whereas significant positive associations were observed with NEU (p < 0.001; 95% CI, 0.000 to 0.109)

Table 1: Demographic and clinical characteristics of patients with AIS

Clinical characteristics	Non-OSA group (N = 56)	OSA group, AHI ≥ 15 (N = 33)	*p value* [a]
Age, $\bar{\chi}$ (s)	59.57 (14.24)	56.09 (12.18)	0.244
Male, N (%)	39 (69.64)	30 (90.91)	0.020
BMI, M (IQR)	24.22 (3.44)	26.20 (4.50)	0.001
Risk factors, N (%)			
Hypertension	37 (66.07)	27 (81.82)	0.110
Diabetes mellitus	16 (28.57)	19 (57.56)	0.007
Hyperlipidemia	29 (51.79)	16 (48.48)	0.764
Coronary heart disease	7 (12.50)	6 (18.18)	0.464
Atrial fibrillation	7 (12.50)	4 (12.12)	0.958
Transient ischemic attack	13 (23.21)	5 (15.15)	0.360
Hyperuricemia	3 (5.36)	1 (3.03)	0.609
Hyperhomocysteinemia	10 (17.86)	6 (18.18)	0.969
Smoking history	24 (42.86)	20 (60.61)	0.106
Alcohol consumption history	15 (26.79)	10 (30.30)	0.721
Thrombolysis, N (%)	10 (17.86)	3 (9.09)	0.258
TOAST classification, N (%)			0.344
Large artery atherosclerosis	22 (39.29)	9 (27.27)	
Cardioembolism	5 (8.93)	3 (9.09)	
Small-vessel occlusion	26 (46.43)	16 (48.48)	
Other determined etiologies	0 (0)	2 (6.06)	
Undetermined etiology	3 (5.36)	3 (9.09)	
Time from onset to MR, days, M (IQR)	2.00 (4.00)	1.50 (3.00)	0.410
Hematological markers			
Red blood cell, $\bar{\chi}$ (s)	4.59 (0.47)	4.78 (0.63)	0.108
Hematocrit, $\bar{\chi}$ (s)	41.20 (4.12)	42.49 (5.08)	0.198
White blood cell, $\bar{\chi}$ (s)	6.59 (1.62)	7.69 (2.28)	0.011
Neutrophil, $\bar{\chi}$ (s)	4.44 (1.54)	5.28 (2.11)	0.034
Monocyte, M (IQR)	0.41 (0.22)	0.48 (0.16)	0.008
Lymphocyte, $\bar{\chi}$ (s), M, $\bar{\chi}$ (s)	1.80 (0.61)	1.93 (0.52)	0.299
Eosinophil, M (IQR)	0.09 (0.14)	0.14 (0.15)	0.073
Platelet, $\bar{\chi}$ (s)	210.85 (54.43)	226.53 (48.87)	0.183
MPV, M (IQR)	10.70 (1.15)	10.85 (1.18)	0.728
PDW, $\bar{\chi}$ (s)	12.53 (1.79)	12.63 (1.77)	0.790
RDW, M (IQR)	12.80 (0.95)	12.65 (1.00)	0.676
Albumin, mean±SD	39.37 (3.81)	40.55 (4.52)	0.202
D-dimer, M (IQR)	0.32 (0.48)	0.31 (0.56)	0.810
Fibrinogen, M (IQR)	3.24 (0.91)	3.52 (1.26)	0.006
NLR, M (IQR)	2.34 (1.58)	2.60 (1.56)	0.384
PLR, M (IQR)	110.30 (62.96)	108.48 (55.09)	0.721
MLR, M (IQR)	0.23 (0.12)	0.26 (0.15)	0.095
MHR, M (IQR)	0.33 (0.22)	0.42 (0.23)	0.026

Table 1: (continued)

Clinical characteristics	Non-OSA group (N = 56	OSA group, AHI ≥ 15 (N = 33)	*p value* [a]
SII, M (IQR)	466.67 (446.61)	544.34 (494.02)	0.256
SCI, M (IQR)	103.67 (44.14)	108.89 (60.05)	0.324
SIRI, M (IQR)	0.91 (0.86)	1.15 (1.32)	0.066
Sleep characteristics, median (range)			
AHI	—	36.70 (16.10 ~ 64.20)	—
Baseline SpO2	—	93.6% (87~97%)	—
Lowest SpO2	—	75% (30~84%)	—

Abbreviations: OSA: Obstructive Sleep Apnea; $\bar{\chi}$: Mean; s, Standard Deviation; M: Median; IQR: Interquartile Range; BMI: Body Mass Index; TOAST: Trial of Org 10172 in Acute Stroke Treatment; MRI: Magnetic Resonance Imaging. MPV: Mean Platelet Volume; PDW: Platelet Distribution Width; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio; PLR: Platelet to Lymphocyte Ratio; MLR: Monocyte to Lymphocyte Ratio; MHR: Monocyte to High-Density Lipoprotein Ratio; SII: Systemic Immune-Inflammation Index = Neutrophil count × Platelet count / Lymphocyte count; SCI: Coagulation-Inflammation Index = Platelet count × Fibrinogen / White blood cell count; SIRI: Systemic Inflammatory Response Index = Neutrophil count × Monocyte count / Lymphocyte count; AHI: Apnea-Hypopnea Index; SpO2: Blood Oxygen Saturation.

p value [a]: For normally distributed continuous variables, values were derived from *t*-tests; for non-normally distributed continuous variables, values were obtained from Mann-Whitney U tests; for count data variables, values were derived from chi-square tests.

and platelet distribution width (p = 0.048; 95% CI, 0.001 to 0.191) (Table 3).

DISCUSSION

Neuroinflammatory response constitutes a critical pathophysiological mechanism in AIS. Findings from Kim *et al.* indicate that suppression of inflammatory cell activity may mitigate cerebral injury following AIS.[20] However, prior studies examining inflammation-related biomarkers frequently included cases with culprit LAO and not differentiate between anterior and posterior circulation strokes. The presence of culprit LAO is an independent determinant of infarct volume and stroke severity. Anatomical and physiological differences between the anterior and posterior circulations, including vessel origin, vessel diameter, flow velocity, shear stress, and collateral capacity, can result in distinct mechanisms of injury under similar ischemic conditions.[21] Unlike previous investigations, the present study exclusively included patients experiencing first-ever anterior circulation AIS without evidence of culprit LAO, with a confirmed diagnosis of OSA prior to stroke onset. This study design aimed to mitigate confounding from prior cerebrovascular disease, which could obscure the underlying interactions between systemic inflammation and OSA.

Table 2: Infarct volume and neurological function scores in patients with AIS

Clinical characteristics	Non-OSA group (N = 56)	OSA group, AHI≥15 (N = 33)	*p value* [a]
Admission NIHSS, N (%)			0.868*
≤3	25 (44.64)	16 (48.48)	
3-10	24 (42.86)	14 (42.42)	
>10	7 (12.50)	3 (9.09)	
NIHSS score at admission, M (IQR)	4.00 (6.00)	4.00 (6.00)	0.527[#]
Infarct volume, M (IQR)	5.22 (19.65)	2.96 (12.57)	0.262[#]

Abbreviations: M: median; IQR: interquartile range; NIHSS: National Institutes of Health Stroke Scale.

p value [a]: derived from *t*-test for continuous normally distributed variables, [#] Mann-Whitney U test for non-normally distributed variables, and * chi-square test for count data variables.

Table 3: Multiple linear regression analysis of factors associated with infarct volume and NIHSS scores in AIS

Dependent variable	Independent variable	β	t	*p*	β95% confidence interval	
					Lower	Upper
Infarct volume	SII	0.001	3.292	0.002	0.000	0.001
	MPV	0.132	2.214	0.030	0.013	0.251
NIHSS score at admission	Neutrophils	0.208	4.185	<0.001	0.000	0.109
	MLR	-2.027	-3.183	0.002	-3.297	-0.758
	OSA history	-0.391	-2.275	0.026	-0.734	-0.048
	PDW	0.096	2.013	0.048	0.001	0.191

Abbreviations: OSA: Obstructive Sleep Apnea; NIHSS: National Institutes of Health Stroke Scale; SII: Systemic Immuno-Inflammation Index; MPV: Mean Platelet Volume; PDW: Platelet Distribution Width; MLR: Monocyte to Lymphocyte Ratio.

The SII, derived from peripheral lymphocyte, neutrophil, and platelet counts, may reflect three concurrent involvement of thrombotic, inflammatory, and adaptive immune processes. Initially proposed for use in oncology, SII has demonstrated relevance in cardiovascular and cerebrovascular diseases and may serve as an integrated biomarker of systemic immune status in patients with AIS.[22,23] In a prospective study of 85,154 participants without prior cardiovascular or cerebrovascular disease, elevated SII was associated with an increased risk of stroke over a 10-year follow-up period.[24]

The pathophysiological contributions of SII to AIS may be attributed to several mechanisms. Neutrophils (NEU), which are recruited to ischemic tissue within hours of stroke onset, release pro-inflammatory cytokines, reactive oxygen species, and matrix metalloproteinase-9. NEU infiltrate ischemic lesions within hours after AIS, releasing inflammatory mediators that compromise the blood-brain barrier, leading to necrosis and apoptosis within the ischemic core.[25,26] Such activity may precipitate secondary complications, such as cerebral edema, hemorrhagic transformation, and worsening neurological function.[27] In contrast, lymphocytes are considered neuroprotective immunomodulators that may mitigate inflammatory damage following AIS.[28] Platelets, beyond their role in hemostasis, also function as regulators of immune and inflammatory pathways. Activated platelets and platelet-derived microparticles can promote inflammation, oxidative stress, angiogenesis, and cellular proliferation, thereby contributing to the progression of cardiovascular and cerebrovascular pathology.[29] Following AIS, platelet activation may worsen cerebral injury.[30]

Hsu *et al*. reported associations between elevated SII and larger hematoma volumes, poorer Glasgow Coma Scale scores, and unfavorable short-term outcomes.[31] The present study found a significant positive correlation between higher SII values and infarct volume, even after adjusting for potential confounding factors. To the best of current knowledge, this represents the first study to demonstrate a statistically significant association between elevated SII and increased infarct volume specifically among patients with anterior circulation AIS without LAO. Elevated SII may signify a heightened inflammatory response and microvascular damage, contributing to impaired penumbral salvage and infarct extension. These findings underscore the potential clinical utility of SII as an early prognostic biomarker and suggest that early interventions aimed at inflammation control may be beneficials in patients presenting with elevated SII at admission.

However, no significant association was observed between SII and NIHSS scores at admission in this cohort. Previous reports have indicated a correlation between elevated SII and higher NIHSS scores at stroke onset. It is important to note, however, that these studies included a heterogeneous mix of stroke subtypes, including both anterior and posterior circulation strokes, and often did not exclude cases with LAO or recurrent stroke. Additionally, multivariate models in those studies frequently did not adjust for infarct location or large artery disease.[32,33] For example, Fernandez-Garza *et al.* did not specify the interval between symptom

onset and blood sampling. Hou *et al*. did not consistently distinguish between different stroke subtypes or locations in their analysis.[32] Huang *et al*. reported that 32.9 percent of their cohort had LAO, and among those with NIHSS scores > 5, with 42.9 percent had such occlusions.[34] In contrast, the present study exclusively included anterior circulation AIS cases without culprit LAO and ensured that all blood samples were collected within three days of symptom onset. The NIHSS is more reliable for detecting defects related to anterior circulation events and may underestimate severity in posterior circulation strokes. Additionally, SII levels have been shown to vary significantly during the first two weeks post-stroke and may be influenced by age and baseline stroke severity.[35,36] Therefore, further large-scale investigations that control for stroke subtype, lesion location, and timing of biomarker measurement are necessary to determine the prognostic significance of SII in AIS.

Interestingly, the present findings indicated that a history of pre-stroke OSA was not associated with increased infarct volume and was negatively associated with stroke severity in anterior circulation AIS without LAO. Although OSA has been linked to endothelial dysfunction, sympathetic overactivity, arrhythmogenesis, impaired glucose regulation, atherosclerosis, hypertension, hypercoagulability, and microvascular cerebral dysfunction, these pathophysiological alterations do not necessarily translate into more severe stroke symptoms or larger infarct volumes.[37] The current findings diverge from those of earlier studies by focusing solely on patients with a confirmed diagnosis of OSA prior to a first-ever cerebrovascular event. In patients with pre-existing cerebrovascular disease, OSA may arise as a consequence rather than a precursor of stroke, raising the possibility of reverse causality. Recurrent hypoxia and hypercapnia experienced during sleep in patients with OSA may induce cerebral ischemic preconditioning, which has been demonstrated to enhance neurogenesis and angiogenesis following cerebral ischemia.[38] OSA has been associated with improved coronary collateral circulation post-myocardial infarction and enhanced cerebrovascular reactivity following hypercapnic challenges.[39,40] Animal models further support this concept; for instance, rodents exposed to hypoxia-hypercapnia prior to induced ischemia displayed reduced neurological impairment compared to controls.[41] These findings suggest that intermittent hypoxic conditioning in OSA may enhance cerebrovascular reserve, mitigating infarct severity and clinical manifestations in certain stroke subtypes. Prospective studies are warranted to clarify the bidirectional relationship between OSA and stroke pathophysiology.

Platelet indices serve as important biomarkers for evaluating platelet activation and functional status. MPV, an indicator of platelet size, is widely recognized as a marker of platelet activity.[42] PDW, which quantifies variability in platelet size and heterogeneity, is indicative of heterogeneity in platelet production and activation. The current study identified a positive association between MPV and infarct volume, constituting the first known evidence to establish a direct relationship between elevated MPV and increased infarct size in the context of AIS. Larger platelets contain more granules and surface receptors, thereby enhancing thrombogenicity and the risk of vascular events.[43,44] However, the prognostic utility of MPV in AIS remains inconclusive, potentially due to variability in blood sampling times, assay techniques, and the effects of antiplatelet medications.[42,45] In addition, PDW was found to be positively correlated with stroke severity, consistent with prior observations.[46]

This study has several limitations. First, it was a single-center, retrospective study with a relatively small sample size, which may limit generalizability. Second, peripheral blood parameters were measured only at the time of admission, without subsequent dynamic monitoring. Third, the classification of OSA status is a major consideration. In the non-OSA group, the absence of pre-stroke polysomnographic evaluation limited the ability to fully exclude undiagnosed OSA. To mitigate this, we employed a conservative approach by exclusively including patients who both reported no or only occasional snoring and were assessed as low-risk by both the Berlin and STOP-Bang questionnaires. Patients with discordant findings (e.g., no snoring but high-risk questionnaire scores) were excluded to maximize the phenotypic contrast between groups. Nevertheless, the use of questionnaires rather than polysomnography may still be subject to recall bias and misclassification. Furthermore, this study primarily focused on the impact of moderate-to-severe OSA (AHI ≥15); stratified analyses including patients with mild OSA are warranted in future investigations. Finally, due to the retrospective nature of this study, other OSA parameters such as lowest oxygen saturation and rapid eye movement-related OSA severity were not available for analysis. Despite

these limitations, the study contributes valuable clinical insights and may assist in guiding future treatment strategies.

In conclusion, elevated levels of SII and MPV may be independently associated with increased infarct volume in patients with AIS involving the anterior circulation without LAO.-These results highlight the need for further investigation of immunomodulatory interventions in AIS.

However, our findings did not reveal an association between pre-stroke OSA with increased infarct volume or greater stroke severity at presentation. Stratified analyses focusing on patients at high risk for OSA or receiving OSA-directed treatment may help refine intervention timing and optimize clinical intervention.

Future studies should incorporate dynamic monitoring of immune parameters and adopt large-scale, multi-center prospective designs to validate and expand upon these findings. Advancing this line of investigation may facilitate the development of evidence-based strategies to improve functional outcomes and inform individualized care pathways for patients with AIS.

ACKNOWLEDGEMENTS

We are particularly grateful to all the people who have given us help on our article.

DISCLOSURE

Ethics: The study was approved by Ethics Committee of the First Hospital of Hebei Medical University. Written informed consent was obtained from all participants.

Availability of data: All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Financial support: None

Conflict of interest: None

REFERENCES

1. Rosamond W, Flegal K, Furie K, *et al.* Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee [published correction appears in *Circulation* 2010;122(1):e10. Kissela, Bret [corrected to Kissela, Brett]]. *Circulation* 2008;117(4):e25-e146. doi:10.1161/CIRCULATIONAHA.107.187998.
2. Anrather J, Iadecola C. Inflammation and stroke: An overview. *Neurotherapeutics* 2016;13(4):661-70. doi:10.1007/s13311-016-0483-x
3. Vidale S, Consoli A, Arnaboldi M, Consoli D. Postischemic inflammation in acute stroke. *J Clin Neurol* 2017;13(1):1-9. doi:10.3988/jcn.2017.13.1.1
4. van der Meijden PEJ, Heemskerk JWM. Platelet biology and functions: new concepts and clinical perspectives. *Nat Rev Cardiol* 2019;16(3):166-79. doi:10.1038/s41569-018-0110-0
5. Su M, Ouyang X, Song Y. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and monocyte to lymphocyte ratio in depression: A meta-analysis. *J Affect Disord* 2022;308:375-83. doi:10.1016/j.jad.2022.04.038
6. Gong P, Liu Y, Gong Y, *et al.* The association of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and lymphocyte to monocyte ratio with post-thrombolysis early neurological outcomes in patients with acute ischemic stroke. *J Neuroinflammation* 2021;18(1):51. doi:10.1186/s12974-021-02090-6
7. Thareja S, Mandapalli R, Shaik F, *et al*. Impact of obstructive sleep apnea on cardiovascular health: A systematic review. *Cureus* 2024;16(10):e71940. doi: 10.7759/cureus.71940.
8. Amen S, Rasool B, Al Lami BS, *et al.* Obstructive sleep apnea and cardiovascular diseases: A systematic review and meta-analysis of prospective studies. *Cureus* 2024;16(10):e71752. doi: 10.7759/cureus.71752.
9. Baillieul S, Dekkers M, Brill AK, *et al.* Sleep apnoea and ischaemic stroke: current knowledge and future directions. *Lancet Neurol* 2022;21(1):78-88. doi:10.1016/S1474-4422(21)00321-5
10. Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005;172(11):1447-51. doi:10.1164/rccm.200505-702OC
11. Adams HP Jr, Bendixen BH, Kappelle LJ, *et al*. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24(1):35-41. doi:10.1161/01.str.24.1.35
12. Loo G, Koo CY, Zhang J, *et al.* Impact of obstructive sleep apnea on cardiovascular outcomes in patients treated with percutaneous coronary intervention: rationale and design of the sleep and stent study. *Clin Cardiol* 2014;37(5):261-9. doi:10.1002/clc.22261
13. Marshall NS, Wong KK, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea and 20-year follow-up for all-cause mortality, stroke, and cancer incidence and mortality in the Busselton Health Study cohort. *J Clin Sleep Med* 2014;10(4):355-62. doi:10.5664/jcsm.3600
14. Redline S, Yenokyan G, Gottlieb DJ, *et al*. Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. *Am J Respir Crit Care Med* 2010;182(2):269-77. doi:10.1164/rccm.200911-1746OC
15. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann*

Intern Med 1999;131(7):485-91. doi:10.7326/0003-4819-131-7-199910050-00002
16. Abrishami A, Khajehdehi A, Chung F. A systematic review of screening questionnaires for obstructive sleep apnea. *Can J Anaesth* 2010;57(5):423-38. doi:10.1007/s12630-010-9280-x
17. Chung F, Yegneswaran B, Liao P, *et al.* STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008;108(5):812-21. doi:10.1097/ALN.0b013e31816d83e4
18. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: A practical approach to screen for obstructive sleep apnea. *Chest* 2016;149(3):631-8. doi:10.1378/chest.15-0903
19. Gensicke H, Zumbrunn T, Jongen LM, *et al*. Characteristics of ischemic brain lesions after stenting or endarterectomy for symptomatic carotid artery stenosis: results from the international carotid stenting study-magnetic resonance imaging substudy. *Stroke* 2013;44(1):80-6. doi:10.1161/STROKEAHA.112.673152
20. Kim JY, Kawabori M, Yenari MA. Innate inflammatory responses in stroke: mechanisms and potential therapeutic targets. *Curr Med Chem* 2014;21(18):2076-97. doi:10.2174/0929867321666131228205146
21. Li Y, Cai Y, Zhao M, Sun J. Risk factors between intracranial-extracranial atherosclerosis and anterior-posterior circulation stroke in ischaemic stroke. *Neurol Res* 2017;39(1):30-5. doi:10.1080/01616412.2016.1250856
22. Ye Z, Hu T, Wang J, *et al.* Systemic immune-inflammation index as a potential biomarker of cardiovascular diseases: A systematic review and meta-analysis. *Front Cardiovasc Med* 2022;9:933913. doi:10.3389/fcvm.2022.933913
23. Cui Z, Kuang S, Yang X, *et al.* Predictive value of the systemic immune inflammation (SII) index for stroke-associated pneumonia. *Brain Behav* 2023;13(12):e3302. doi:10.1002/brb3.3302
24. Jin Z, Wu Q, Chen S, *et al.* The associations of two novel inflammation indexes, SII and SIRI with the risks for cardiovascular diseases and all-cause mortality: A ten-year follow-up study in 85,154 individuals. *J Inflamm Res* 2021;14:131-40. doi:10.2147/JIR.S283835
25. Chamorro Á, Dirnagl U, Urra X, Planas AM. Neuroprotection in acute stroke: targeting excitotoxicity, oxidative and nitrosative stress, and inflammation. *Lancet Neurol* 2016;15(8):869-81. doi:10.1016/S1474-4422(16)00114-9
26. Darbousset R, Thomas GM, Mezouar S, *et al*. Tissue factor-positive neutrophils bind to injured endothelial wall and initiate thrombus formation. *Blood* 2012;120(10):2133-43. doi:10.1182/blood-2012-06-437772
27. Petty MA, Lo EH. Junctional complexes of the blood-brain barrier: permeability changes in neuroinflammation. *Prog Neurobiol* 2002;68(5):311-23. doi:10.1016/s0301-0082(02)00128-4
28. Liesz A, Suri-Payer E, Veltkamp C, *et al*. Regulatory T cells are key cerebroprotective immunomodulators in acute experimental stroke. *Nat Med* 2009;15(2):192-9. doi:10.1038/nm.1927
29. Khodadi E. Platelet function in cardiovascular disease: Activation of molecules and activation by molecules. *Cardiovasc Toxicol* 2020;20(1):1-10. doi:10.1007/s12012-019-09555-4
30. Nording HM, Seizer P, Langer HF. Platelets in inflammation and atherogenesis. *Front Immunol* 2015;6:98. doi:10.3389/fimmu.2015.00098
31. Hsu HT, Chen PY, Tzeng IS, Hsu PJ, Lin SK. Correlation of immune-inflammatory markers with clinical features and novel location-specific nomograms for short-term outcomes in patients with intracerebral hemorrhage. *Diagnostics* (Basel) 2022;12(3):622. doi:10.3390/diagnostics12030622
32. Hou D, Wang C, Luo Y, *et al*. Systemic immune-inflammation index (SII) but not platelet-albumin-bilirubin (PALBI) grade is associated with severity of acute ischemic stroke (AIS). *Int J Neurosci* 2021;131(12):1203-8. doi:10.1080/00207454.2020.1784166
33. Fernández-Garza LE, González-Aquines A, Botello-Hernández E, Pérez-Vázquez G, Cristobal-Niño M, Góngora-Rivera F. Segmented neutrophil-to-monocyte ratio and systemic immune-inflammation index associated with the severity and functional prognosis of acute ischemic stroke. *Int J Neurosci* 2025;135(2):228-36. doi:10.1080/00207454.2023.2294705
34. Huang L. Increased systemic immune-inflammation index predicts disease severity and functional outcome in acute ischemic stroke patients. *Neurologist* 2023;28(1):32-8. doi:10.1097/NRL.0000000000000464
35. Adiguzel A, Arsava EM, Topcuoglu MA. Temporal course of peripheral inflammation markers and indexes following acute ischemic stroke: prediction of mortality, functional outcome, and stroke-associated pneumonia. *Neurol Res* 2022;44(3):224-31. doi:10.1080/01616412.2021.1975222
36. Mureșan EM, Golea A, Vesa ȘC, Lenghel M, Csutak C, Perju-Dumbravă L. Emergency department point-of-care biomarkers and day 90 functional outcome in spontaneous intracerebral hemorrhage: A single-center pilot study. *Exp Ther Med* 2022;23(3):200. doi:10.3892/etm.2022.11123
37. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353(19):2034-41. doi:10.1056/NEJMoa043104
38. Lee SH, Kim YJ, Lee KM, Ryu S, Yoon BW. Ischemic preconditioning enhances neurogenesis in the subventricular zone. *Neuroscience* 2007;146(3):1020-31. doi:10.1016/j.neuroscience.2007.02.058
39. Steiner S, Schueller PO, Schulze V, Strauer BE. Occurrence of coronary collateral vessels in patients with sleep apnea and total coronary occlusion. *Chest* 2010;137(3):516-20. doi:10.1378/chest.09-1136
40. Ryan CM, Battisti-Charbonney A, Sobczyk O, *et al*. Evaluation of cerebrovascular reactivity in subjects with and without obstructive sleep apnea. *J Stroke Cerebrovasc Dis* 2018;27(1):162-8. doi:10.1016/j.jstrokecerebrovasdis.2017.08.015
41. Tregub P, Kulikov V, Motin Y, Bespalov A, Osipov

I. Combined exposure to hypercapnia and hypoxia provides its maximum neuroprotective effect during focal ischemic injury in the brain. *J Stroke Cerebrovasc Dis* 2015;24(2):381-7. doi:10.1016/j.jstrokecerebrovasdis.2014.09.003

42. Farah R, Samra N. Mean platelets volume and neutrophil to lymphocyte ratio as predictors of stroke. *J Clin Lab Anal* 2018;32(1):e22189. doi:10.1002/jcla.22189
43. Martin JF, Kristensen SD, Mathur A, Grove EL, Choudry FA. The causal role of megakaryocyte–platelet hyperactivity in acute coronary syndromes. *Nat Rev Cardiol* 2012;9(11):658-70. doi:10.1038/nrcardio.2012.131
44. O'Malley T, Langhorne P, Elton RA, Stewart C. Platelet size in stroke patients. *Stroke* 1995;26(6):995-9. doi:10.1161/01.str.26.6.995
45. Ot S, Zafar L, Beg M, Siddiqui OA. Association of mean platelet volume with risk factors and functional outcome in acute ischemic stroke. *J Neurosci Rural Pract* 2021;12(4):764-9. doi:10.1055/s-0041-1735326
46. Sarkar RN, Das CK, Bhattacharjee U, Banerjee M. Platelet indices as a marker of severity in non-diabetic non hypertensive acute ischemic stroke patients. *J Assoc Physicians India* 2018;66(7):40-2.