RESEARCH ARTICLE

Hypersensitive C-reactive protein-albumin ratio in endovascular treatment of acute ischaemic stroke clinical prognostic value

Youde Cai[1], Zhongyong Peng[2], Xiong Zheng[3], Fang Gan[4], Qiansong He[5], Yunzhi Chen[6]

Abstract

Objective: To determine the specific quantitative relationship between the hypersensitive C-reactive protein-albumin ratio and short-term clinical outcome measures within 30 days of endovascular therapy in patients diagnosed with acute ischaemic stroke.

Method: The retrospective study was conducted at the Jinyang Hospital, China, and comprised data from January 2019 to July 2023 of patients with acute large-vessel occlusive stroke who underwent endovascular therapy. The patients were stratified into two prognostic groups according to their 30-day postoperative modified Rankin Scale scores. Group A had patients with score 0-2 indicating good prognosis, and group B had patients with score 3-6 indicating poor prognosis. Baseline characteristics, vascular risk factors, laboratory test parameters, consultation duration, stroke subtype, responsible vessel and other relevant clinical data was noted and compared between the groups. Data was analysed using SPSS 25.

Results: Of the 195 patients, 125(64%) were males and 70(36%) were females. The overall median age was 65 years (interquartile range: 54-74 years). There were 102(52.3%) patients in group A and 93(47.7%) were in group B. Advanced age, hypertension, cerebral oedema, haemorrhagic transformation, baseline National Institutes of Health Stroke score, white blood cell count, infarct volume and hypersensitive C-reactive protein-albumin ratio were significantly different between the groups ($p<0.05$). Receiver operating characteristic curve analysis revealed that C-reactive protein-albumin ratio predicted the highest value with area under the curve being 0.778.

Conclusion: Elevated hypersensitive C-reactive protein-albumin ratio levels independently correlated with adverse clinical outcomes in acute ischaemic stroke patients undergoing endovascular therapy.

Keywords: Hypersensitive C-reactive protein-albumin ratio, Endovascular treatment of acute, Acute ischaemic stroke, Prognostic. (JPMA 75: 1732; 2025) **DOI: https://doi.org/10.47391/JPMA.21269**

Introduction

Endovascular therapy (EVT) has been substantiated as an efficacious intervention for the amelioration of clinical outcomes in acute ischaemic stroke (AIS) patients. However, the clinical prognosis after ECT is influenced by several factors.[1] Serum inflammatory markers have garnered attention for their pivotal role in AIS pathophysiology and their utility as biological indicators for AIS assessment.[2]

C-reactive protein (CRP) and albumin (ALB) serve as acute-phase proteins and are integral to the acute temporal physiological response.[3] Existing literature indicates that hypersensitive C-reactive protein (hs-CRP) partakes in multiple aspects of cerebral infarction development, such as platelet activation, thrombogenesis, plaque dislodgment, and vascular remodelling. Consequently, hs-CRP is recognised as an independent risk factor for ischaemic stroke and is predictive of stroke severity, recurrence, neurological function deterioration, and poor prognosis.[4] On the other hand, ALB functions beyond its role as a nutritional index; it is also a critical prognostic indicator for stroke severity, recurrence, neurological function, and overall outcome. This is mainly attributable to its roles in maintaining colloidal osmotic pressure, exerting antioxidant effects, facilitating drug transport, and other biological functions. Moreover, ALB has been shown to have neuroprotective properties, such as mitigating neuronal damage, scavenging free radicals, and minimising reperfusion injury.[5]

Recent empirical research has elucidated a correlation between the hs-C-reactive protein/ALB ratio (CAR) and post-ischaemic neurological deficits, indicating a potentiating effect.[6] However, the current body of literature addressing the prognostic value of CAR in the context of EVT for AIS is notably scant. The current study was planned to investigate the predictive role of CAR on prognosis after

[1]Department of Neurology, Graduate School, Guizhou University of Traditional Chinese Medicine, Guiyang, China; [2]Department of Neurology, The Affiliated Jinyang Hospital of Guizhou Medical University, Guiyang, China; [3]Cardiovascular Disease Centre, Baiyun Hospital of Guizhou Medical University, Guiyang, China; [4]Clinical Research Centre, Guizhou Provincial Orthopaedic Hospital, Guiyang, China [5]Guizhou University of Traditional Chinese Medicine, Guiyang, China; [6]Graduate School, Guizhou University of Traditional Chinese Medicine, Guiyang, China.

Correspondence: Yunzhi Chen. e-mail: chenyunzhiz70@gzy.edu.cn

ORCID ID: 0009-0005-7841-331X

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endovascular treatment of AIS.

Materials and Methods

The retrospective study was conducted from January 2019 to June 2024 at the Jinyang Hospital, Guizhou Medical University, China, and comprised data from January 2019 to July 2023 of consecutively enrolled patients who experienced AID with large-vessel occlusion and underwent EVT at the Emergency and Neurology departments. After approval from the institutional ethics review committee, the sample size was calculated using PASS15.0 software, adhering to a non-probabilistic consecutive sampling design, and meeting the minimum requirements for sample size estimation and the Events Per Variable principle.[7]

Those included were patients aged >18 years in whom preoperative computed tomography angiography (CTA) or digital subtraction angiography (DSA) confirmed occlusion in either anterior or posterior circulation, had National Institutes of Health Stroke Scale (NIHSS) score ≥6 and modified thrombolysis in cerebral infarction (mTICI) score 3.[8-9] Informed consent was obtained from all the patients.

Those excluded were patients with residual sequelae of prior stroke, specifically assessed using the modified Rankin Scale (mRS) with a preoperative mRS score >2.[10] Also excluded were those with chronic occlusion in large arteries of either the anterior or posterior circulation before intervention, concurrent cerebral haemorrhage, active infection, rheumatic immune diseases and /or malignancy before surgery. Case with incomplete clinical data or absence of 30-day postoperative follow-up were also excluded.

They were stratified into two prognostic groups according to their 30-day postoperative mRS scores. Group A had patients with score 0-2 indicating good prognosis, and group B had patients with score 3-6 indicating poor prognosis.

Standard demographic characteristics, including age and gender, were extracted from structured electronic medical record（ EMR） fields. Vascular risk factors, such as hypertension (HTN), diabetes mellitus (DM), dyslipidaemia, atrial fibrillation and current smoking status, were manually verified by two independent researchers to ensure consistency with source documents. Additional clinical data included the presence of intravenous (IV) thrombolysis, the time elapsed from admission to puncture and from puncture to recanalisation, baseline NIHSS scores, Trial of Org10172 in Acute Stroke Treatment (TOAST) classification, and responsible vasculature.[11] Laboratory data and disease characteristics, such as cerebral oedema and symptomatic intracranial haemorrhage, were also collated. Fasting venous blood samples were taken immediately on admission, and 30-day mRS score outcomes were recorded upon discharge. The levels of hs-CRP and ALB were measured using standardised assays, with institutional reference ranges defined as albumin 40-55g/L and hs-CRP 0-5mg/L. Elevated hs-CRP (>3mg/L) and hypoalbuminaemia (<40g/L) were classified as abnormal.

Data was analysed using SPSS 25. Categorical data was presented as frequencies and percentages, and was assessed using chi-square test. Continuous data underwent normality testing. Data not conforming to a normal distribution was evaluated using the rank sum test and expressed as median with interquartile range (IQR), whereas those with normal distribution were subjected to a t-test and expressed as mean±standard deviation. P<0.05 was considered statistically significant.

Multifactorial logistic regression was employed to perform regression analyses. The CAR was analysed as a continuous variable, with the odds ratio (OR) reflecting the risk per 1-unit increase in CAR. Variables with $p<0.05$ in univariate analyses were included in multivariable logistic regression. To avoid multicollinearity, only the composite biomarker CAR and not its individual components were included in the multivariate model, as CAR inherently reflects both inflammatory and anti-inflammatory pathways. A stepwise backward elimination approach was applied to retain variables with $p<0.05$ in the final model. Multicollinearity was assessed using variance inflation factors (VIF), with VIF<5 considered acceptable. Model fit was evaluated via the Hosmer-Lemeshow test ($p>0.05$). Receiver operating characteristic (ROC) curves were plotted to assess the predictive validity of the parameters through the calculation of the area under the ROC curve (AUC).

Results

Of the 458 patients initially evaluated, 212(46.3%) underwent EVT for AIS and achieved complete reperfusion. Of them, 17(8%) cases were excluded; 6(35.3%) had preoperative mRS >2, 5(29.4%) had preoperative chronic large-vessel occlusion, 3(17.6%) had combined cerebral haemorrhage, and 3(17.6%) had incomplete data. The study was completed by 195(92%) patients; 125(64%) males and 70(36%) females. The overall median age was 65 years (IQR: 54-74 years). There were 102(52.3%) patients in group A and 93(47.7%) were in group B. Univariate analysis revealed significant differences between the groups with respect to HTN, atrial fibrillation, cerebral oedema, intracranial haemorrhage, age, baseline NIHSS score, blood glucose levels, leukocyte and platelet counts, time from

Table-1: Univariate analysis of baseline characteristics (n=195).

Characteristics	Total (n=195） [n (%)]	Favourable outcome (mRS30 0-2) (n=102) [n (%)]	Unfavourable outcome (mRS30 3-6) (n=93) [n (%)]	*p*-value
Demographics				
Age (years)	65.00 [54.00;74.00]	61.00 [51.00;68.75]	71.00 [63.00;78.00]	<0.001*
Gender, male	125(64.10)	67 (65.69%)	67 (65.69%)	0.629
Smoking	91(46.67)	51 (50.00%)	40 (43.01%)	0.329
Hypertensive	119(61.03)	49 (48.04%)	70 (75.27%)	<0.001*
Diabetes	37 (18.97)	15 (14.71%)	22 (23.66%)	0.111
Atrial fibrillation	68 (34.87)	28 (27.45%)	40 (43.01%)	0.023
Clinical feature				
Intravenous thrombolysis	98 (50.26)	54 (52.94%)	44 (47.31%)	0.432
Hydrocephalus	100(51.28)	33 (32.35%)	67 (72.04%)	<0.001*
Bleeding conversion	79 (40.51)	17 (16.67%)	62 (66.67%)	<0.001 *
Infarct volume (ml)	11.50 [1.91;30.40]	4.55 [1.10;14.07]	22.80 [10.10;48.60]	<0.001*
TOAST subtype	-	-	-	0.360
Large-artery atherosclerosis	117 (60.00)	64 (62.75%)	53 (56.99%)	-
Cardioembolism	58 (29.74)	26 (25.49%)	32 (34.41%)	-
Other determined aetiology	20 (10.26)	12 (11.76%)	8 (8.60%)	-
Responsible vessels	-	-	-	0.824
ICA or MCA or ACA	138(70.77)	74 (72.55%)	64 (68.82%)	-
VA or BA	44 (22.56%)	22 (21.57%)	22 (23.66%)	-
Tandem lesion	13 (6.67%)	6 (5.88%)	7 (7.53%)	-
NIHSS	14.00 [10.00;18.50]	12.00 [8.00;14.75]	17.00 [13.00;20.00]	<0.001*
Time from arrival to puncture， min	67.00 [45.00;108.00]	61.50 [42.25;109.75]	68.00 [49.00;105.00]	0.233
Puncture to recanalisation time， min	50.00 [40.00;67.50]	46.00 [37.00;60.00]	58.00 [45.00;75.00]	0.002*
Laboratory examinations				
Glucose, (mg/dl)	126(108-1653.7)	119.16(100.6-144.5)	139.86(114.4-163.6)	0.001*
Creatinine, (mg/dl)	0.83(0.71-1.02)	0.81(0.72;1.01)	0.84(0.71;1.05)	0.542
Haemoglobin (g/L)	133.67 (21.33)	135.73±19.15	131.42±23.39	0.160
white blood cell count (10^9/L)	8.20 [6.64;10.41]	7.60 [6.36;9.70]	8.82 [7.30;11.42]	0.003*
Platelet count,(10^9/L)	198.00 [158.50;249.50]	211.00 [172.25;262.75]	188.00 [152.00;243.00]	0.023*
PT,s	13.40 [13.00;14.30]	13.40 [13.00;14.20]	13.40 [13.00;14.50]	0.435
APTT,s	34.70 [32.05;38.10]	35.25 [33.05;37.77]	33.90 [30.70;38.60]	0.114
Fibrinogen, (g/L)	3.16 [2.62;3.90]	3.12 [2.65;3.75]	3.20 [2.61;4.09]	0.358
Total cholesterol, (mg/dl)	173.6(146.9;196.4)	175.1(148.4;198.3)	171.6(14.03;196.5)	0.266
Triglyceride, (mg/dl)	113.3(86.7;171.8)	149.7(86.7;171.8)	114.2(85.9;170.9)	0.862
Low-Density lipoprotein Cholesterol, (mg/dl)	104.02(81.9;123.7)	109.0(89.3;128.7)	97.0(76.5;121.4)	0.069
Homocysteine (μmol/dl)	1.74(1.39;2.29)	1.69(1.32;2.35)	1.82(1.48;2.22)	0.621
hs-CRP, (g/L)	1.83 [1.02;3.68]	1.44 [0.89;1.94]	3.62 [1.49;10.29]	<0.001*
Albumin, (g/L)	41.00 [37.98;44.49]	41.85 [38.52;44.80]	40.46 [37.00;43.60]	0.014*
CAR	4.24 [2.50;8.64]	3.38 [2.13;4.63]	8.43 [3.78;23.87]	<0.001*

mRS30: Modified Rankin Scale, ICA: Internal carotid artery, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, VA: Vertebral artery, BA: Basilar artery, TOAST: Trial of Org 10172 in Acute Stroke Treatment classification, NIHSS, National Institutes of Health Stroke Scale, PT: Prothrombin time, APTT: Activated partial thromboplastin time, hs-CRP: Hypersensitive C-reactive protein, CAR: C-reactive protein-albumin ratio; *p<0.05.

puncture to recanalisation, infarct volume, hs-CRP, ALB and CAR (p<0.05) (Table 1).

Multivariate logistic regression analysis demonstrated that HTN, cerebral oedema, intracranial haemorrhage, age, NIHSS score, leukocyte count, infarct volume and CAR were independent predictors (Table 2). No significant multicollinearity was observed among the variables (p>0.05), and an adequate model fit was confirmed (p=0.612).

ROC curve analysis revealed that CAR predicted the highest value (AUC=0.778) (Figure).

Discussion

The aetiology of ischaemic stroke is intricate, with the acute phase predominantly influenced by factors, such as excitatory glutamate release, cellular infiltration by

Table-2: Multivariate logistic regression analysis of independent predictors of unfavourable 30-day outcome.

	p-value	OR	OR (95%)	
			lower limit	upper limit
Hypertensive	0.038#	3.837	1.076	13.678
Atrial fibrillation	0.987	1.011	0.279	3.659
Hydrocephalus	0.007#	6.733	1.690	26.829
Bleeding conversion	0.004#	6.060	1.773	20.711
Age，years	0.023#	1.068	1.009	1.130
NIHSS	0.007#	1.175	1.046	1.320
Glucose (mg/dl)	0.185	1.190	0.920	1.541
white blood cell count (10^9/L)	0.039#	1.272	1.013	1.598
Platelet count (109/L)	0.291	0.995	0.987	1.004
Puncture to recanalisation time (min)	0.080	1.014	0.998	1.030
Infarct volume (ml)	0.017#	1.038	1.007	1.071
CAR	0.001#	1.281	1.111	1.476

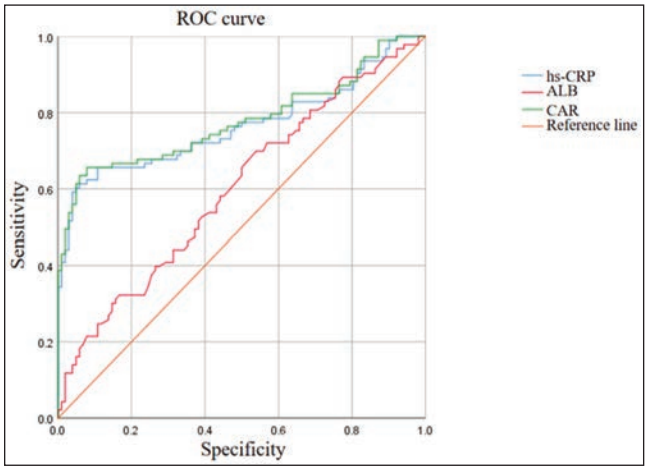

Figure: Comparison of ROC curves of ALB (AUC=0.602), hs-CRP (AUC=0.765), and CAR (AUC=0.778). CAR demonstrated the highest predictive ability for 30-day outcomes in acute ischaemic stroke patients.
ROC: Receiver operating characteristic, AUC: Area under the curve, ALB: Albumin, CAR: C-reactive protein-albumin ratio.

inflammatory components, oxidative stress and programmed cell death or apoptosis. Notably, the inflammatory response is critical in this context.[12] Upon the disruption of environmental homeostasis, pro-inflammatory cytokines, specifically interleukin-6 (IL-6) and interferon beta (INF-β), are released into the circulatory system. These cytokines instigate neuroendocrine modifications and target hepatic and extrahepatic tissues, culminating in the augmented secretion of acute-phase proteins within 24-48 hours.[13] CRP and ALB are acute-phase proteins integral to the acute-phase response.[14] During this response, positive acute-phase reactants experience an elevation, whereas negative acute-phase reactants show a decline. These reactants establish a homeostatic balance between pro-inflammatory and anti-inflammatory actions.[15] While individual biomarkers offer some insights, they are subject to variability due to internal and external environmental influences, limiting their capacity to portray the post-ischaemic stroke immune-inflammatory status comprehensively. As a result, composite markers that encapsulate multiple facets of the inflammatory response could serve as more reliable indicators.

Extensive research corroborates the association between inflammation and both the onset and prognosis of ischaemic stroke.[16] In this regard, hs-CRP, an acute-phase reactant, has garnered attention as a sensitive marker of inflammation. It is implicated in the initiation and progression of atherosclerosis, and its elevated levels are tightly correlated with the instability of atherosclerotic plaques and stroke-related outcomes.[17] Apart from neutralising free radicals, ALB significantly contributes to inhibiting platelet activation and aggregation while diminishing blood viscosity. A state of hypoproteinemia induces lipid and coagulation factor synthesis, thereby escalating hyperlipidaemia and hypercoagulability, and further promoting the formation of atherosclerotic plaques.[18] The CAR has been rigorously evaluated and deemed a robust predictive and diagnostic marker. It is increasingly recognised as a surrogate marker for disease severity and offers reliable prognostic insights.[19]

The current study aimed at scrutinising the biological attributes of hs-CRP and ALB, focussing on their correlation with the clinical outcomes following endovascular treatment of AIS. Baseline data for 30-day prognosis showed that CAR levels were elevated in the cohort with poor prognostic outcomes compared to the favourable prognosis group. ROC curve analysis revealed that CAR possessed predictive validity for 30-day clinical outcomes in EVT patients, outperforming hs-CRP and ALB individually. The area under the ROC curve was 0.778, with specificity 92.2% and sensitivity 65.6%. This underscores CAR's substantial predictive utility. CAR offers an integrative perspective by combining the pro-inflammatory properties of hs-CRP with the anti-inflammatory characteristics of ALB. As such, CAR stands as a comprehensive biomarker, proficiently encapsulating the severity and likely prognostic outcomes of AIS.

According to extant literature, CAR has a discernible impact on the 30-day prognosis of AIS. Specifically, hs-CRP contributes to the pathogenesis of cerebral infarction and amplifies the necrotic damage to brain tissue. Conversely, distinguished by its unique terminal structure, ALB mitigates oxidative-induced neuronal damage and exerts an antioxidant protective effect that curtails neuronal damage.[20] During the acute phase of cerebral infarction, hs-CRP and other inflammatory markers reciprocally induce a series of inflammatory responses, exacerbating reperfusion injury to the cerebral tissue. In this context, ALB

plays a protective role by elevating plasma colloid osmolality, thereby preventing hypotension-induced hypoperfusion cerebral infarction.[21] ALB is integral in maintaining intracranial osmolality and facilitates improved perfusion in locally ischaemic tissues. It also opposes microcirculatory embolism and attenuates reperfusion injury, thereby mitigating damage to brain tissue. Notably, hs-CRP levels can peak expeditiously in response to inflammatory stimuli, whereas a decline in ALB levels serves as a countermeasure to elevated acute-phase reactive proteins.[22]

In the acute phase, hs-CRP and ALB interact to establish a balance between pro-inflammatory and anti-inflammatory processes. Due to its substantial osmotic capacity, localised inflammation alters vascular permeability, prompting ALB to translocate into both vascular and interstitial spaces. This action effectively neutralises inflammation and mitigates damage to the surrounding, unaffected tissues. Additionally, the presence of inflammatory markers, such as hs-CRP, during the onset of acute cerebral infarction compromises the structural integrity of the infarcted tissue. This compromise manifests as increased tissue permeability and local oedema. As a primary osmotic agent, ALB infiltrates the tissue interstitial space, inhibiting the infiltration of inflammatory factors into the peri-infarct region. This action restricts the propagation of inflammatory responses to local normal tissues and ameliorates cerebral oedema in the post-infarct period.[23] As an inflammatory marker, hs-CRP serves as a prognostic indicator, particularly pertinent for the 30-day clinical outcomes of patients undergoing endovascular therapy for AIS.

The current study identified multiple variables that had an impact on neurological recovery and clinical prognosis following EVT in AIS patients, like age, HTN, cerebral oedema, intracranial haemorrhage, NIHSS score, leukocyte count, and infarct volume, which was in line with literature.[24] However, despite the statistical significance of these variables, the CAR demonstrated superior predictive utility. ROC analysis showed that CAR achieved the highest AUC (0.778) compared to hs-CRP or ALB alone, underscoring its unique role as a composite biomarker integrating both inflammatory and anti-inflammatory/ nutritional pathways. While hs-CRP and albumin were significant in univariate analyses, CAR was retained in the multivariate model due to its integrative nature, which minimises redundancy and improves predictive efficiency compared to isolated biomarkers. This is consistent with previous studies suggesting that CAR, by combining the pro-inflammatory effect of hs-CRP and the neuroprotective properties of ALB, provides a more holistic reflection of the pathophysiological state in AIS patients.[25] The elderly demographic manifests an elevated prevalence of comorbidities, a trend that escalates with advancing age. There is a progressive decline in cardiorespiratory function and a potential deterioration in cerebral collateral circulation. HTN, cerebral oedema and haemorrhagic transformation have been definitively linked with an unfavourable prognosis post-AIS.[26] Specific complications engendered by hypertension include reperfusion injury, secondary cerebral oedema and haemorrhage.

Furthermore, intracranial hyperperfusion emerges as a severe complication after endovascular treatment for AIS.[27] The baseline NIHSS score is a salient prognostic indicator, with elevated scores correlating with poorer clinical outcomes.[28] Following the initial onset of AIS, complement-activated platelets induce the expression of P-selectin, initiating the leukocyte recruitment cascade, thereby amplifying the inflammatory response.[29]

Elevated leukocyte counts have been implicated in the formation of unstable plaques. They are consequential in initiating acute embolic events, identifying them as a significant risk factor for developing AIS.[30] The dimension of the core infarct exhibits a robust correlation with AIS prognosis; notably, smaller core infarct sizes are associated with a more favourable clinical outcome. Conversely, larger core infarcts elevate the risk of haemorrhagic transformation post-EVT and are indicative of a deteriorating clinical prognosis. Recent evidence suggests that patients may still benefit from EVT, even in extensive core infarcts.[31] In the present study, factors, including atrial fibrillation, blood glucose levels, platelet count and time elapsed from puncture to recanalisation did not significantly correlate with the 30-day prognosis of AIS, a phenomenon attributed to an insufficient sample size.

Hyperglycaemia was verified as a pertinent indicator of neurological decline, potentially linked to ensuing reperfusion injuries. Atrial fibrillation serves as a considerable risk factor for cardiogenic embolism, contributing to haemodynamic instability that increases the propensity for embolic events in both systemic and pulmonary circulations. These embolic events are inclined to occur preferentially within the internal carotid artery system. Embolisms instigated by atrial fibrillation tend to manifest as extensive infarcts and exhibit a greater susceptibility to haemorrhagic transformation. This observation could be correlated to an elevated risk of proximal vascular occlusion and a heightened incidence rate of intracranial haemorrhagic transformation in patients who experience large ischaemic strokes precipitated by atrial fibrillation.

The current study has several limitations due to its retrospective design. First, the single-centre nature of the data may have introduced selection bias and limited the generalisability of the findings. Second, unmeasured confounders may have influenced the results, although known covariates were adjusted for. Third, reliance on baseline CAR measurements may have overlooked dynamic changes in the inflammatory status during the 30-day follow-up, which could have refined prognostic accuracy. Finally, the exclusion of patients with incomplete follow-up could further bias the results towards survivors with better compliance.

Conclusion

Elevated CAR levels independently correlated with adverse clinical outcomes in AIS patients undergoing EVT.

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Author Contribution:

YC, ZP & XZ: Writing, review, editing, drafting, formal analysis, data curation and concept.
FG: Drafting, funding acquisition, visualization and formal analysis.
QH: Data curation and concept.
YC: Writing, review, editing, methodology and concept.