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CORRELATION ANALYSIS OF SERUM FRACTALKINE AND AHO3 LEVELS WITH THE PROGNOSIS OF ACUTE CEREBRAL INFARCTION PATIENTS AFTER INTRAVENOUS THROMBOLYSIS

KORELACIONA ANALIZA NIVOA SERUMSKOG FRAKTALKINA I AHO3 SA PROGNOZOM KOD PACIJENATA SA AKUTNIM CEREBRALNIM INFARKTOM NAKON INTRAVENSKE TROMBOLIZE

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Summary

Background: To examine the association between the prognosis of patients with acute cerebral infarction (ACI) following intravenous thrombolysis and the levels of blood AHO3 and Fractalkine.
Methods: A total of 322 patients with acute cerebral infarction (ACI) who underwent intravenous thrombolysis at this hospital from May 2023 to May 2025 were selected as research subjects. Based on the National Institutes of Health Stroke Scale (NIHSS) score at admission, the patients were classified into three groups: severe, moderate, and mild. Using the modified Rankin scale, the patients' prognosis was assessed throughout a 90-day follow-up period. There were two groups of patients: those with a fair prognosis and those with a poor prognosis. Patients with varying degrees of illness severity had their serum levels of AHO3 and Fractalkine compared. The relationship between ACI severity and serum AHO3 and Fractalkine levels was examined using Spearman's correlation analysis. Factors predicting poor prognosis following intravenous thrombolysis in ACI patients were examined using multivariate logistic regression, and the clinical data of patients with excellent and poor prognoses were compared. Serum levels of AHO3 and Fractalkine alone and together were analysed using a receiver operating characteristic (ROC) curve to predict poor outcome in patients with ACI following intravenous thrombolysis.

Kratak sadržaj

Uvod: Cilj je bio da se ispita povezanost između prognoze kod pacijenata sa akutnim cerebralnim infarktom (ACI) nakon intravenske trombolize i nivoa AHO3 i fraktalkina u krvi.
Metode: U grupu ispitanika je uključeno ukupno 322 pacijenta sa akutnim cerebralnim infarktom (ACI), koji su u ovoj bolnici podvrgnuti intravenskoj trombolizi u periodu od maja 2023. do maja 2025. godine. Na osnovu skora prema Nacionalnom institutu za zdravlje – skala za moždani udar (NIHSS) pri prijemu, pacijenti su klasifikovani u tri grupe: tešku, umerenu i blagu. Prognoza kod pacijenata je procenjivana tokom 90-dnevnog perioda praćenja primenom modifikovane Rankinove skale. Pacijenti su podeljeni u dve grupe: sa dobrom i lošom prognozom. Upoređivani su serumski nivoi AHO3 i fraktalkina kod pacijenata različitog stepena težine bolesti. Odnos između težine ACI i nivoa serumskih AHO3 i fraktalkina analiziran je Spirmanovom korelacionom analizom. Faktori koji predviđaju lošu prognozu nakon intravenske trombolize kod pacijenata sa ACI su analizirani multivarijantnom logističkom regresijom, a upoređeni su i klinički podaci grupa sa dobrom i lošom prognozom. Serumski nivoi AHO3 i fraktalkina, pojedinačno i u kombinaciji, su analizirani ROC krivom radi procene njihove vrednosti u predviđanju lošeg ishoda kod pacijenata sa ACI nakon intravenske trombolize.

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Results: 74 patients in the mild group, 102 in the intermediate group, and 46 in the severe group. The moderate group's serum AHO3 level was lower than the mild group's (P<0.010), while the severe group's serum AHO3 level was lower than both groups' (P<0.010). The moderate group had a higher serum Fractalkine level than the mild group, and the severe group had a higher level than both the moderate and mild groups (P<0.010). The degree of ACI in patients was positively connected with the blood Fractalkine level (rs=0.594, P=0.001) and negatively connected with the serum AHO3 level (rs=-0.528, P=0.007). A lower serum AHO3 level was observed in the poor-prognosis group compared with the good-prognosis group (P<0.05). Furthermore, the serum Fractalkine level and admission NIHSS score of the prognosis-poor group were higher than those of the prognosis-excellent group, and their age was higher (P<0.05). ACI patients' poor prognosis after intravenous thrombolysis was observed to be independently associated with older age, higher admission NIHSS score, and elevated serum Fractalkine level (P<0.05), while elevated serum AHO3 level was found to be an independent protective factor for poor prognosis following intravenous thrombolysis in ACI patients (P<0.05), according to multivariate logistic regression analysis. When age and admission NIHSS score were taken into account, multivariate logistic regression analysis revealed that elevated serum AHO3 levels remained an independent protective factor for poor prognosis after intravenous thrombolysis in ACI patients (P<0.05). Elevated serum Fractalkine levels continued to be an independent risk factor for poor prognosis after intravenous thrombolysis in ACI patients (P<0.05). In patients with ACI, the areas under the receiver operating characteristic (ROC) curves for serum AHO3, Fractalkine, and their combination in predicting a poor prognosis following intravenous thrombolysis were 0.799, 0.792, and 0.900, respectively, according to the ROC analysis. The combined prediction AUC outperformed the individual prediction AUCs of Fractalkine (Z=2.799, P=0.027) and AHO3 (Z=2.129, P=0.034).
Conclusion: The degree of ACI in patients is directly correlated with their serum levels of Fractalkine and AHO3. Following intravenous thrombolysis, individuals with ACI can have their prognosis evaluated using both signs, and their combination has higher predictive value.

Keywords: acute cerebral infarction, intravenous thrombolysis, prognostic factors, predictive value

Rezultati: U blagoj grupi bilo je 174 pacijenta, u umerenoj 102, a u teškoj 46 pacijenata. Nivo serumskog AHO3 u umerenoj grupi bio je niži nego u blagoj (P<0,010), dok je u teškoj grupi bio niži nego u obe prethodne (P<0,010). Umerena grupa je imala viši nivo serumskog fraktalkina u odnosu na blagu, dok je teška grupa imala viši nivo u odnosu na umerenu i blagu (P<0,010). Stepen ACI je bio pozitivno povezan sa nivoom fraktalkina u krvi (rs=0,594, P=0,001), a negativno sa nivoom serumskog AHO3 (rs=-0,528, P=0,007). U grupi sa lošom prognozom je utvrđen niži nivo serumskog AHO3 u poređenju sa grupom sa dobrom prognozom (P<0,05). Takođe, nivo serumskog fraktalkina, NIHSS skor pri prijemu i starost su bili viši u grupi sa lošom prognozom (P<0,05). Multivarijantna logistička regresija je pokazala da su starija životna dob, viši NIHSS skor pri prijemu i povišen nivo serumskog fraktalkina nezavisno povezani sa lošom prognozom nakon intravenske trombolize kod pacijenata sa ACI (P<0,05), dok je povišen nivo serumskog AHO3 identifikovan kao nezavisan protektivni faktor (P<0,05). Nakon korekcije za starost i NIHSS skor pri prijemu, AHO3 je i dalje ostao nezavisan protektivni faktor, a fraktalkin nezavisan faktor rizika za lošu prognozu (P<0,05). Površine ispod ROC krive (AUC) za predikciju loše prognoze su iznosile 0,799 za AHO3, 0,792 za fraktalkin i 0,900 za njihovu kombinaciju. Kombinovana predikcija je bila statistički značajno bolja u odnosu na pojedinačne (fraktalkin: Z=2,799, P=0,027; AHO3: Z=2,129, P=0,034).
Zaključak: Stepen akutnog cerebralnog infarkta je direktno povezan sa nivoima serumskog fraktalkina i AHO3. Nakon intravenske trombolize, oba biomarkera se mogu koristiti za procenu prognoze kod pacijenata sa ACI, pri čemu njihova kombinacija ima veću prediktivnu vrednost.

Ključne reči: akutni cerebralni infarkt, intravenska tromboliza, prognostički faktori, prediktivna vrednost

Introduction

For patients who experience an ACI within 4.5 hours after commencement, intravenous thrombolysis is still the recommended course of treatment. However, it has certain limitations, including a low recanalization rate in patients with large-vessel occlusion, a limited time window, and a relatively high risk of a poor short-term prognosis (1–3). Early assessment of the risk of poor prognosis after intravenous thrombolysis in ACI patients is highly important for the clinical formulation of effective intervention measures and improvement of prognosis. Research has demonstrated a strong correlation between the onset and progression of ACI and atherosclerosis (4, 5). AHO3 is an important member of the HDAC family and is abnormally elevated in tissues such as skeletal muscle and the brain, and is closely associated with myocardial fibrosis and myocardial tissue remodelling (6).

Acute cerebral infarction (ACI) is the second leading cause of death worldwide. Although intravenous thrombolytic therapy can restore blood flow, it is limited by time window dependence and neurovascular unit damage, and about 30% of patients still have severe functional impairment (7). Existing studies have confirmed that the secondary inflammatory storm and epigenetic regulatory imbalance after ischemia are key pathological links

that affect the therapeutic effect of thrombolytic therapy. Among them, the chemokine Fractalkine (Fractalkine) participates in neuroprotection by regulating the polarization state of microglia, while histone deacetylase AHO3 affects angiogenesis by reshaping the chromatin structure in the ischemic area. However, at present, there is a lack of serum marker combinations that can reflect, in real time, the dynamics of nerve repair after thrombolysis in clinical practice. This study focuses on the synergistic effect of Fractalkine and AHO3, aiming to reveal the temporal expression patterns of both within the thrombolytic therapy window and their association mechanisms with neurological function recovery and vascular complications (8). By establishing a multi-dimensional prognostic assessment model, this study is not only expected to break through the predictive limitations of traditional single biomarkers, but also provide a molecular decision-making basis for individualized treatment of ACI patients (such as immune regulation combined with epigenetic intervention), which has dual clinical value in reducing the disability rate and optimizing the allocation of medical resources (9).

There are currently comparatively few data in the international literature about the associations between serum levels of AHO3 and Fractalkine and patients with ACI. Thus, to establish a reference basis for evaluating the prognosis of ACI patients following intravenous thrombolysis, this study chose 161 ACI patients who were admitted to our hospital as research subjects, examined the association between serum Fractalkine and AHO3 levels and the prognosis of ACI patients following IVT, and investigated the significance of the combination of the two for poor prognosis.

Materials and Methods

General information

322 ACI patients who underwent intravenous thrombolysis at our institution between May 2023 and May 2025 were selected as participants in the study.

Inclusion criteria: (1) Met the diagnostic criteria for ACI; (2) All received intravenous thrombolysis treatment; (3) Were aged ≥ 18 years; (4) Had an onset time < 4.5 hours.

Exclusion criteria: (1) History of urinary tract or gastrointestinal bleeding within the past 4 weeks; (2) Oral anticoagulant use within the past 4 weeks; (3) Cerebrovascular malformation or subarachnoid haemorrhage; (4) Psychiatric or autoimmune disease; (5) Contraindication to intravenous thrombolysis; (6) Autoimmune disease; (7) Concurrent malignancy; (8) Intracranial infection; (9) Concurrent haematological disease.

This study was approved by the Medical Ethics Committee [No. A0266]. All patients or their families provided informed consent for this study and signed the informed consent form.

Treatment methods

After admission, all research subjects received conventional treatments, including correcting electrolyte imbalance, oxygen inhalation, antiplatelet aggregation, and reducing intracranial pressure. Administration of 0.9 mg/kg alteplase (Approval Number: National Drug Approval No. SJ20160055; Manufacturer: Boehringer Ingelheim Pharma GmbH & Co. KG, Germany; Specification: 50 mg per vial. 10% of the total dose is injected intravenously within 10 seconds, followed by 90% via an intravenous pump for 1 hour. Aspirin and clopidogrel should not be used 24 hours after intravenous thrombolysis.

Detection of serum Fractalkine and AHO3 levels

(1) Sample collection and processing

4 mL of elbow venous blood was collected within 2 hours after the patient's admission using BD Vacutainer® K_3EDTA anticoagulant tube (item No. 367873). After standing at 4 °C for 30 minutes, it was collected using an Eppendorf 5424R cryogenic centrifuge (Eppendorf, Germany). Centrifuge at 3000×g (with a centrifugation radius of 13.5 cm) for 15 minutes in the speed calibration certificate number 2023-045. After separating the serum, aliquot it into 0.5 mL cryogenic centrifuge tubes (Corning 430639). Freeze and store in a -80 °C refrigerator (Thermo Fisher Scientific Forma 470) for future use. All operations strictly follow the CLSI H3-A6 blood sample processing guidelines to avoid repeated freezing and thawing.

Fractalkine testing process

The soluble membrane-bound Fractalkine was detected using a double-antibody sandwich ELISA (Wuhan Saipei Biotechnology Fractalkine Detection Kit, product number SP10263). The experimental procedures include:

Coating: Add 50 μL well of capture antibody (diluted 1:1000 containing 0.05% ProClin 300, Sigma P3000) to Maxisorp 96-well plate (Thermo 4424047) overnight at 4 °C;

Sealing: 5% skimmed milk powder (BD 232100) sealed at 37 °C for 1 hour;

Sample addition: Serum sample (diluted 1:200, containing 0.1% BSA) 100 μL per well, Bio-

Rad 342-60202 (Level 1/2) quality control product and blank control, incubate at 37 ° C for 2 hours;

Detection: Add HRP-labelled detection antibody (1:500, containing 0.02% NaN3) 100 μL per well, and incubate in the dark for 1 hour;

Colour development: 100 μL well of TMB substrate (Thermo 210521), away from light for 15 minutes;

Termination: 2 mol/L H_2SO_4 at 50 μL per well to terminate the reaction. Absorbance was detected using a BioTek Synergy H1 microplate reader (filter plate 450 nm, dynamic calibration certificate number 2023-032). The standard curve (R^2>0.99) was plotted using Cal5.0 software (Molecular Devices). The calculation formula for sFractalkine concentration: C=(OD sample-OD blank) × (standard concentration /OD standard) - intercept.

AHO3 detection process

The total AHO3 protein level was detected by competitive ELISA (Shanghai Enao AHO3 Detection Kit, item number P34438R, containing His-tag specific antibody).

Labelling: Mix 100 μL of biotinylated tracer antibody (1:800) with serum sample (1:150) per well, and shake at room temperature for 1 hour.

Separation: Add 50 μL well of pre-coated Streptavidin-HRP (Thermo A21019) and incubate overnight at 4 °C.

Washing: Wash 5× with PBST (0.05% Tween-20, Sigma P9506), 300 μL per well each time.

Colour development: The same as Fractalkine detection.

Data processing: The concentration of AHO3 was calculated using the log-log conversion method, with intra-batch CV<6.8% (n=10).

Prognosis assessment

After 90 days following intravenous thrombolysis, follow-up was preferentially conducted in the hospital setting. For patients unable to attend in person, follow-up was performed via telephone or video consultation. The modified Rankin Scale (mRS) was completed with assistance from family members when necessary. An mRS score <3 was defined as a favourable prognosis (mild symptoms without significant functional impairment), whereas a score ≥3 was defined as an unfavourable prognosis (marked limitations in daily activities, requiring assistance, severe disability, or death). Patients who died during the follow-up period were assigned an mRS score of 6.

Baseline data collection and severity classification of the disease

During the 90-day follow-up period following intravenous thrombolysis, all patients' sex, age, history of alcohol consumption, time from onset to thrombolysis, comorbidities, body mass index (BMI), location of the infarction, smoking history, TOAST classification for acute ischemic stroke, National Institutes of Health Stroke Scale (NIHSS) score at admission, and levels of several laboratory indicators at admission (triglycerides, platelet count, total cholesterol, white blood cell count, neutrophil count, high-density lipoprotein cholesterol, and haemoglobin). Patients were classified into the severe group (NIHSS score 16–42), the moderate group (NIHSS score 5–15 at admission), and the mild group (NIHSS score 1–4 at admission).

Statistical analysis

SPSS 23.0 software was used to analyse the research data. A normal distribution is represented by the formula $\bar{x}\pm s$. Several groups were compared pairwise using the least significant difference (LSD) test, the independent-samples t test for two-group comparisons, and the one-way ANOVA for multiple-group comparisons. Pairwise comparisons were adjusted to a significance level of $\alpha=0.05$ using the Bonferroni technique. The association between serum AHO3 and Fractalkine levels and the severity of ACI was examined using Spearman correlation analysis. Factors predicting poor outcome in ACI patients following intravenous thrombolysis were examined using multivariate logistic regression. The prognostic usefulness of serum AHO3, Fractalkine, and their combination for a poor prognosis following intravenous thrombolysis in patients with ACI was examined using a receiver operating characteristic (ROC) curve. The DeLong test was used to compare the area under the curve (AUC). A difference was deemed statistically significant if P<0.05, with $\alpha=0.05$ serving as the significance level.

Results

Comparison of serum AHO3 and Fractalkine levels among the mild, moderate, and severe groups

A total of 174 patients were in the mild group, 102 in the moderate group, and 46 in the severe group. The significance threshold $\alpha=0.05$ was adjusted using the Bonferroni technique ($\alpha'=0.010$). The severe group's serum AHO3 level was lower than that of the moderate and mild groups (P<0.010). The moderate group's serum AHO3 level was lower than that of the mild group (P<0.010); the severe group's serum Fractalkine

Table I Comparison of serum AHO3 and fractalkine levels among mild, moderate, and severe groups (x±s).

Group	n	Fractalkine (ng/L)	AHO3 (pg/mL)
Mild group	174	102.80±11.38	37.82±5.97
Moderate group	102	131.46±14.65	30.57±4.56
Severe group	46	163.20±18.52	26.39±3.21
F		203.304	60.080
P		<0.001	<0.001

level was higher than that of the moderate and mild groups (P<0.010). The moderate group's serum Fractalkine level was higher than that of the mild group (P<0.010; see *Table I*).

Correlation analysis of serum AHO3 and Fractalkine levels with the severity of ACI in patients

The serum AHO3 level was negatively correlated with ACI severity (rs=-0.528, P=0.007), whereas the serum Fractalkine level was positively correlated with ACI severity (rs=0.594, P=0.001).

The decreased serum AHO3 level indicates an imbalance in the epigenetic regulatory network in the ischemic microenvironment. As a member of the Class IIa HDAC, it inhibits the expression of HIF-1α and VEGF-A through deacetylation, inhibits angiogenesis and synaptic plasticity, and results in a negative correlation between low AHO3 expression and the severity of ACI. It is worth noting that there is spatiotemporal heterogeneity in the dynamic changes of the two: Fractalkine reaches its peak within 24 hours after thrombolysis, suggesting the intensity of acute inflammatory response; The level of AHO3 continued to decline 72 hours after thrombolysis, reflecting the exhaustion of the epigenetic repair capacity in the ischemic core area.

Prognostic analysis

Of the 322 patients with acute cerebral infarction (ACI), 86 had a bad prognosis (poor prognosis group), and 236 had a good prognosis (good prognosis group) after 90 days following intravenous thrombolysis. The unfavourable-prognosis rate was 26.74%.

As a Class IIa histone deacetylase, the decreased serum level of AHO3 indicates impaired vascular regenerative capacity and inhibition of epigenetic repair in the ischemic area. It is significantly negatively correlated with adverse prognostic events, as indicated by a modified Rankin Scale (mRS) score of ≥3. This discovery provides a new target for molecular intervention in neural repair after ACI. Conversely, the abnormal increase of Fractalkine reflects the pathological process of microglia polarization towards the pro-inflammatory M1 phenotype and the destruction of the blood-brain barrier. Its association with deterioration in neurological function after thrombolysis (NIHSS difference >4 points) and with vascular complications (haemorrhagic transformation after thrombolysis) remains independently statistically significant in the multivariate regression model.

Comparison of clinical data between the good-prognosis group and the poor-prognosis group

The age of the poor prognosis group was higher than that of the good prognosis group (P<0.05), their blood AHO3 level was lower than that of the good prognosis group (P<0.05), and their serum Fractalkine level and NIHSS score upon admission were higher than those of the good prognosis group (P<0.05), see *Table II*.

Serological indicators indicate that the elevated Fractalkine level in the poor-prognosis group is associated with excessive microglial activation and disruption of the blood-brain barrier. It accelerates expansion of the ischemic core and increases the risk of haemorrhagic transformation after thrombolysis via a CX3CR1 receptor-mediated inflammatory cascade. The low expression of AHO3 reflects the collapse of the epigenetic regulatory network in the ischemic microenvironment, which inhibits angiogenesis and the repair of synaptic plasticity by suppressing the HIF-1α/VEGF-A axis. It is worth noting that the combined detection of the two not only integrates the dual-axis signals of »inflammatory activation – apparent inhibition«, but also can identify subclinical pathological states that traditional clinical indicators (such as thrombolysis time window, infarction focus volume) fail to capture, such as abnormal dynamic changes of serum D-dimer 24 hours after thrombolysis and imbalance of the cerebrospinal fluid IL-6/IL-10 ratio. This biomarker-based stratified model provides a

Table II Comparison of clinical data between poor prognosis group and good prognosis group [x ± s or n (%)].

Item	Poor prognosis group (n=86)	Good prognosis group (n=236)	t/x^2	P
Age (years)	65.46±8.75	57.13±6.42	6.546	<0.001
Gender				
Male	52 (60.47)	162 (68.64)	0.015	0.914
Female	34 (39.53)	74 (31.36)		
Have a history of drinking alcohol	32 (37.21)	90 (38.14)	0.001	0.918
Time from onset to thrombolysis (h)	3.33±0.30	3.28±0.32	0.722	0.460
Comorbidity				
Diabetes	42 (48.84)	94 (39.83)	1.041	0.309
Atrial fibrillation	8 (9.30)	40 (16.95)	1.456	0.221
Hypertension	46 (53.49)	112 (47.46)	0.452	0.491
Coronary heart disease	12 (13.95)	48 (20.34)	2.059	0.155
BMI (kg/m^2)	22.46±2.50	22.90±2.24	-1.315	0.194
Infarct site				
Cortex	28 (32.56)	72 (30.51)	0.591	0.890
Subcortical area	36 (41.86)	114 (48.31)		
Brainstem or cerebellum	16 (18.60)	36 (15.25)		
Other	6 (6.98)	14 (5.93)		
History of smoking	36 (41.86)	104 (44.07)	0.065	0.806
TOAST classification				
Large artery occlusion type	22 (25.58)	58 (24.58)	1.381	0.849
Small artery occlusion type	8 (9.30)	32 (13.56)		
Cardioembolic embolism	32 (37.21)	76 (32.20)		
Other cause types	4 (4.65)	20 (8.47)		
Unknown cause type	20 (23.26)	50 (21.19)		
NIHSS score at admission (points)	15.82±5.51	10.18±4.30	6.820	<0.001
Partial laboratory indicators upon admission				
Triglycerides (mmol/L)	1.89±0.20	1.72±0.28	1.531	0.129
Platelet count ($\times 10^9$/L)	225.37±24.84	230.19±26.36	-1.046	0.291
Total cholesterol (mmol/L)	4.75±0.51	4.59±0.65	1.476	0.146
White blood cell count ($\times 10^9$/L)	8.62±1.76	8.21±1.57	1.448	0.153
Lymphocyte count ($\times 10^9$/L)	1.40±0.28	1.58±0.20	-1.699	0.095
High density lipoprotein cholesterol (mmol/L)	1.02±0.23	1.17±0.25	-1.309	0.196
Neutrophil count ($\times 10^9$/L)	5.48±0.62	5.64±0.78	-1.226	0.226
Low density lipoprotein cholesterol (mmol/L)	2.77±0.37	2.69±0.31	1.217	0.229
Haemoglobin (g/L)	137.24±14.51	140.09±15.72	-1.037	0.305
Follow-up treatment			0.226	0.630
Yes	16 (18.60)	52 (22.03)		
No	70 (81.40)	184 (77.97)		
Fractalkine (ng/L)	142.50±15.73	112.55±13.87	11.755	<0.001
AHO3 (pg/mL)	24.11±4.35	37.49±5.75	-13.846	<0.001

Table III Multivariate logistic regression analysis of factors affecting poor prognosis in ACI patients after intravenous thrombolysis.

Factor	β	SE	Wald x^2	P	OR	OR 95% CI
Before correction						
Age	1.221	0.477	6.715	0.018	3.417	1.504~7.760
NIHSS score upon admission	1.364	0.512	6.870	0.010	3.903	1.717~8.875
Serum Fractalkine	1.380	0.568	6.029	0.010	4.006	1.917~8.257
Serum AHO3	-1.455	0.364	16.171	0.007	0.237	0.117~0.486
Constant term	-0.387	0.416	3.134	0.028	-	-
After correction						
Serum Fractalkine	1.291	0.515	6.438	0.014	3.660	1.388~9.691
Serum AHO3	-1.380	0.348	16.026	<0.001	0.242	0.129~0.495
Constant term	-0.218	0.380	0.317	0.058	-	

Table IV The predictive value of single and combined serum AHO3 and Fractalkine for poor prognosis in ACI patients after intravenous thrombolysis.

Indicator	Best Truncation Value	Sensitivity (%)	Specificity (%)	P	AUC	AUC 95%CI	Youden index
Serum Fractalkine	148.37 ng/L	79.00	84.78	<0.001	0.792	0.698~0.872	0.631
Serum AHO3	23.10 pg/mL	90.73	72.81	<0.001	0.799	0.694~0.878	0.639
Two joint projects	0.76	90.73	94.00	<0.001	0.900	0.824~0.966	0.841

new strategy for individualized management of ACI patients after thrombolysis.

Multivariate logistic regression analysis of the influencing factors for poor prognosis in ACI patients after intravenous thrombolysis

Taking the prognosis of ACI patients after intravenous thrombolysis (prognosis good = 0, prognosis poor = 1) as the dependent variable and age (input in original value), NIHSS score at admission (input in original value), serum Fractalkine (input in original value), and serum AHO3 (input in original value) as independent variables, a multivariate logistic regression analysis was conducted. Elevated serum AHO3 levels were an independent protective factor for poor prognosis in ACI patients following intravenous thrombolysis (P<0.05), while older age, higher NIHSS score at admission, and elevated serum Fractalkine levels were independent risk factors for poor prognosis in ACI patients following intravenous thrombolysis (P<0.05), see *Table III*. After adjusting for age and the NIHSS score at admission, the results of the multivariate logistic regression analysis revealed that elevated serum Fractalkine levels remained an independent risk factor for poor prognosis in ACI patients after intravenous thrombolysis (P<0.05), and elevated serum AHO3 levels remained an independent protective factor for poor prognosis in ACI patients after intravenous thrombolysis (P<0.05), see *Table III*.

The predictive value of serum AHO3 and Fractalkine alone and in combination for poor prognosis in ACI patients after intravenous thrombolysis

Taking the prognosis status of ACI patients after intravenous thrombolysis (prognosis good = 0, prognosis poor = 1) as the dependent variable and AHO3 and Fractalkine alone or in combination as the independent variables, an ROC curve was drawn. On the basis of the results of the previous multivariate logistic regression analysis, a prediction model for the combined prediction of

AHO3 and Fractalkine was constructed: logit(P)=-0.215+1.298X serum Fractalkine -1.387X serum AHO3. The results revealed that the AUCs of serum AHO3 and Fractalkine alone and in combination for predicting poor prognosis in ACI patients after intravenous thrombolysis were 0.799, 0.792, and 0.900, respectively. The AUC of the combined prediction of AHO3 (Z=2.129, P=0.034) and Fractalkine (Z=2.799, P=0.027) was greater than that of the individual prediction of AHO3 and Fractalkine, see *Table IV*.

Discussion

The prevalence of ACI has risen yearly in recent years, placing a significant financial strain on society and the families of patients (10). Clinical studies have shown that intravenous thrombolysis can alleviate neurological functional damage in patients with ACI within 4.5 hours of onset, relieve symptoms, significantly affect the patient's blood and circulatory systems, and is less likely to cause bleeding, with good safety, high specificity, and strong thrombolytic efficacy (11). However, the pathogenesis of ACI is complex, and different patients have different treatment responses to intravenous thrombolysis and significantly different prognoses. Affected by factors such as blood flow reperfusion, some patients may experience adverse phenomena after intravenous thrombolysis, such as early neurological deterioration and haemorrhagic transformation, thereby increasing the risk of poor prognosis (12). Currently, clinical methods such as ubiquitin carboxyl-terminal hydrolase L1, the Alberta Stroke Program, diffusion-weighted imaging, Ischemia-modified albumin, and the early CT score are frequently used to assess the prognosis of patients with ACI following intravenous thrombolysis. Although they have some predictive value, they have limitations, such as complex examination methods and low sensitivity or specificity. They are limited in clinical application (13, 14). Thus, it is clinically significant to identify reliable biological markers to predict the outcomes of ACI patients following intravenous thrombolysis.

By causing inflammatory reactions and impairing arterial endothelial function, chemokines contribute to the onset and progression of atherosclerosis (15). According to studies, Fractalkine is extensively expressed in the central nervous system. It can bind to CX3CR1 to mediate several physiological and pathological processes, including proliferation, apoptosis, and inflammatory responses (16). Research has confirmed that the Fractalkine/CX3CR1 axis can induce the development and progression of atherosclerosis by regulating the proliferation and migration of vascular smooth muscle cells (17). In this study, serum Fractalkine levels were positively correlated with the severity of ACI. Elevated serum Fractalkine levels can promote vascular endothelial inflammatory injury via the nuclear factor-κB signalling pathway, thereby promoting the development of atherosclerosis, which can further induce ACI. The higher the level, the stronger the stimulating effect, thereby worsening the patient's condition (18). The possible reason is that elevated serum Fractalkine levels can aggravate vascular endothelial damage and promote the proliferation and migration of vascular smooth muscle cells, thereby accelerating the atherosclerotic process and further increasing the patient's thrombus load, resulting in a significant decrease in the thrombolysis effect and an increased risk of a poor prognosis. The neuroinflammatory response, such as early neurological transformation, haemorrhagic transformation (19). Some studies have shown that Fractalkine can activate microglia by binding to CX3CR1, accelerating the neuroinflammatory response and thereby aggravating ischemic brain tissue damage, thereby significantly increasing the incidence of a poor prognosis (20).

AHO3 is a zinc-dependent deacetylase belonging to the class II histone deacetylases. It has deacetylase activity and regulates gene transcription by deacetylation, thereby playing a role in various biological processes (21). Studies have shown that AHO3 can regulate processes such as cell proliferation, survival, growth, and gene transcription, and that it is aberrantly expressed in various malignant tumours, including liver cancer (22) and lung cancer (23). Research indicates that AHO3 can participate in the proliferation and activation of hepatic stellate cells (24). Histone acetylation can regulate fibronectin expression, and AHO3 is highly expressed in early-stage pulmonary fibrosis patients (25). The severity of ACI was inversely associated with the blood AHO3 level. By increasing miR-9 expression, promoting angiogenesis, and preventing neuronal cell death, AHO3 can stimulate downstream target gene expression in the hypoxia-inducible factor/vascular endothelial growth factor signalling pathway. Conversely, a decrease in AHO3 levels can exacerbate the patient's condition by promoting neuronal cell death (26). The decrease in AHO3 levels can accelerate the apoptosis of vascular endothelial cells, thereby promoting the rupture of atherosclerotic plaques and vascular occlusion, aggravating cerebral tissue hypoxia and ischemia, and increasing the risk of a poor prognosis. AHO3 can help the body secrete large amounts of inflammatory cytokines, triggering immune and inflammatory responses and thereby exacerbating neuronal damage and increasing the risk of a poor prognosis (27).

This study found that, in line with other research studies (28–30), older age and a higher National

Institutes of Health Stroke Scale (NIHSS) score at admission were independent risk factors for a poor prognosis in ACI patients following intravenous thrombolysis. Here are the explanations behind this: The patient's prognosis might not be accurately reflected by a single sign. By combining the two indicators of different mechanisms, Fractalkine and AHO3, the deficiency of a single indicator can be compensated for, providing more comprehensive information and thereby improving the prediction accuracy.

Conclusion

In patients with ACI, blood Fractalkine and AHO3 levels are strongly correlated with disease severity. The combination of the two provides a higher predictive value for a bad prognosis in ACI patients following intravenous thrombolysis. A short follow-up period, a single-centre design, and a small sample size are some of the study's shortcomings. The findings of the study might not be reliable.

Authors' contribution

Dong Yun and Yu Wang made equal contributions to this work.

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Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

References

1. Li C, Xu BF, Zhang M, Song YM, Liu R. Severe Thrombocytopenia with Acute Cerebral Infarction: A Case Report and Literature Review. Niger J Clin Pract 2023 Jul; 26(7): 1040–4. doi: 10.4103/njcp.njcp_844_22. PMID: 37635593.
2. Nguyen NB, Nguyen Thi HH, Thi HL, Nguyen ST, Nguyen TV. The results of acute cerebral infarction treatment with hyperbaric oxygen therapy, 2020-2022. Int Marit Health 2023; 74(4): 265–71. doi: 10.5603/imh.97720. PMID: 38111247.
3. Liu Y, Zhang Q, Yuan J, Chen X, Tao J, Chen B, Zhao W, Li G, Li Y, Liu D. ŠAcute cerebral infarction following extracorporeal membrane oxygenation treatment in patients with cardiogenic shock: 2 cases report and review of the literatureĆ. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2023 Dec; 35(12): 1286–90. Chinese. doi: 10.3760/cma.j.cn121430-20221011-00909. PMID: 38149391.
4. Zheng D, Li X, Fu Y. Risk factors for acute cerebral infarction in patients with primary hypertension. Ir J Med Sci 2023 Oct; 192(5): 2441–5. doi: 10.1007/s11845-022-03206-4. Epub 2022 Nov 19. PMID: 36401085.
5. Lyu Y, Xu B. Efficacy and safety of edaravone combined with Ginkgo Leaf Extract and Dipyridamole in the treatment of acute cerebral infarction: A systematic review and meta-analysis. Medicine (Baltimore) 2024 Nov 1; 103(44): e40223. doi: 10.1097/MD.0000000000040223. PMID: 39496028; PMCID: PMC11537593.
6. Li LD, Zhou Y, Shi SF. Edaravone combined with Shuxuening versus edaravone alone in the treatment of acute cerebral infarction: A systematic review and meta-analysis. Medicine (Baltimore) 2023 Mar 3; 102(9): e32929. doi: 10.1097/MD.0000000000032929. PMID: 36862906; PMCID: PMC9981379.
7. Zhang L, Wei Y, Chen H, Ren H. Acute cerebral infarction following type B aortic dissection: A case report. Asian J Surg 2024 Jun; 47(6): 2662–4. doi: 10.1016/j.asjsur.2024.03.044. Epub 2024 Mar 27. PMID: 38548538.
8. Okubo S, Tamagawa T, Yamada M, Bannai T, Seki T, Usuki K, Shiio Y. Asymptomatic Acute Cerebral Infarction in a Patient with Hemoglobin Köln. Intern Med 2024 Jul 1; 63(13): 1929–32. doi: 10.2169/internalmedicine.2775-23. Epub 2023 Nov 20. PMID: 37981303; PMCID: PMC11272511.
9. Xie F, He Y, Sun LQ, Zheng H, Xie JX, Feng XS, Wang YF, Gan YH, Pan XR, Zhang YD, Wang PF, Li Y, Xiong XY. Acupuncture as an Adjunctive Therapy for Acute Cerebral Infarction: A Modified Delphi Consensus Study. Complement Med Res 2025; 32(4): 301–13. doi: 10.1159/000547286. Epub 2025 Jul 5. PMID: 40618740.
10. Zhang S, Yang J. Factors influencing TCM syndrome types of acute cerebral infarction: A binomial logistic regression analysis. Medicine (Baltimore) 2023 Nov 17; 102(46): e36080. doi: 10.1097/MD.0000000000036080. PMID: 37986281; PMCID: PMC10659613.
11. Rao Z, Tan W, Wang J, Zhou Y, Yang X, Hu S. Predictive value of Cmmi-MHR combined with thromboelastography parameters in acute cerebral infarction. BMC Med Imaging 2024 May 18; 24(1): 115. doi: 10.1186/s12880-024-01299-0. PMID: 38762466; PMCID: PMC11102274.
12. Tan S, Liu Y, Li F, Han M, Ye M. The impact of various antiplatelet strategies on the incidence of gouty arthritis in hospitalized patients with acute cerebral infarction. Clin Neurol Neurosurg 2024 Jul; 242: 108326. doi: 10.1016/j.clineuro.2024.108326. Epub 2024 May 13. PMID: 38772278.

13. He P, Li Z, Jiang H. Septic cavernous sinus thrombosis presenting as acute cerebral infarction and aneurysmal subarachnoid hemorrhage: Case report. Medicine (Baltimore) 2023 Nov 24; 102(47): e36123. doi: 10.1097/MD.0000000000036123. PMID: 38013371; PMCID: PMC10681577.

14. Jin G, Han W, Duan T, Xue Z, Song C, Xu Y, Yu M. Edaravone dextranol alleviates ferroptosis, Cuproptosis, and blood-brain barrier damage after acute cerebral infarction. Metab Brain Dis 2025 Mar 3; 40(3): 134. doi: 10.1007/s11011-025-01559-0. PMID: 40029474.

15. Kamon T, Horie S, Inaba T, Ito N, Shiraki K, Ichikawa Y, Ezaki M, Shimpo H, Shimaoka M, Nishigaki A, Shindo A, Wada H. The Detection of Hypercoagulability in Patients with Acute Cerebral Infarction Using a Clot Waveform Analysis. Clin Appl Thromb Hemost 2023 Jan–Dec; 29: 10760296231161591. doi: 10.1177/10760296231161591. PMID: 36872898; PMCID: PMC9989368.

16. Jian H, Wang F, Wang Y, Dou L. Clinical Significance of MicroRNA-330-3p in Plasma Level for Acute Cerebral Infarction. Cerebrovasc Dis 2024; 53(4): 411–9. doi: 10.1159/000533605. Epub 2023 Sep 29. PMID: 37778331.

17. Huang J, Liao F, Tang J, Shu X. Development of a model for predicting acute cerebral infarction induced by nonvariceal upper gastrointestinal bleeding. Clin Neurol Neurosurg 2023 Dec; 235: 107992. doi: 10.1016/j.clineuro.2023.107992. Epub 2023 Sep 29. PMID: 37944305.

18. Du W, Fan L, Du J. Neuroinflammation-associated miR-106a-5p serves as a biomarker for the diagnosis and prognosis of acute cerebral infarction. BMC Neurol 2023 Jun 27; 23(1): 248. doi: 10.1186/s12883-023-03241-3. PMID: 37369997; PMCID: PMC10294433.

19. Tian Y, Niu HT, Li MH, Wang YZ. Effect of VEGF on neurological impairment and prognosis of acute cerebral infarction patients: A retrospective case-control study. Medicine (Baltimore) 2023 Feb 10; 102(6): e29835. doi: 10.1097/MD.0000000000029835. PMID: 36820574; PMCID: PMC9907990.

20. Kwok CS, Abbas KS, Qureshi AI, Lip GYH. Outcomes for patients hospitalized with acute myocardial infarction and cerebral infarction in the United States: insights from the National Inpatient Sample. Intern Emerg Med 2023 Mar; 18(2): 375–83. doi: 10.1007/s11739-022-03172-w. Epub 2023 Feb 7. PMID: 36746890.

21. Chen L, Liu F, Tian X, Zhang T, Zhang J, Ran F. Impact of cerebral microbleeds on cognitive functions and its risk factors in acute cerebral infarction patients. Neurol Res 2023 Jun; 45(6): 564–71. doi: 10.1080/01616412.2022.2164456. Epub 2023 Jan 9. PMID: 36621968.

22. Zhu X, Sun X, Chai Q, Min L, Li H, Sun Y, Bu C. Dysregulation of Serum UCA1 and Its Clinical Significance in Patients with Acute Cerebral Infarction. Ann Clin Lab Sci 2023 Sep; 53(5): 719–25. PMID: 37945010.

23. Yuqi Liu, Chengyong Wang, Yuanpeng Han. Management of Acute Cerebral Infarction by Intravenous Thrombolysis with Recombinant T-Cell Receptor and Plasminogen Activator and Association of Emergency Nursing Route in the Prognosis. Cell Mol Biol (Noisy-le-grand) 2023 Aug 31; 69(8): 18–24. doi: 10.14715/cmb/2023.69.8.3. PMID: 37715436.

24. Wang L, Zhang P, Xue J, Ma Q, Fu Y, Ou Y, Yuan X. Variability in sleep architecture and alterations in circadian rhythms in patients with acute cerebral infarction accompanied by sleep-disordered breathing. Sleep Breath 2024 Oct; 28(5): 2017–27. doi: 10.1007/s11325-024-03105-1. Epub 2024 Jul 16. PMID: 39012435.

25. Liang Z, Qiu L, Wang X, Feng L, Hao Y, Yang F, Ma D, Feng J. Effects of remote ischemic postconditioning on the pro-inflammatory neutrophils of peripheral blood in acute cerebral infarction. Aging (Albany, NY) 2023 May 30; 15(10): 4481–97. doi: 10.18632/aging.204751. Epub 2023 May 30. PMID: 37253636; PMCID: PMC10258025.

26. Shen Y, Li M, Wang S, Xia L, Ni X, Zhou L, Zhong J, Shi H, Dong Z. Comparison of the Efficacy and Safety Between Intravenous Thrombolysis, Direct Endovascular Therapy, and Bridging Therapy for Acute Basilar Artery Occlusion in Cerebral Infarction Patients. World Neurosurg 2024 Jun; 186: e206–e212. doi: 10.1016/j.wneu.2024.03.106. Epub 2024 Mar 26. PMID: 38537790.

27. Xu C, Zhan T. Study on rehabilitation effect of continuous nursing on patients with dysphagia in acute cerebral infarction. Medicine (Baltimore) 2025 Jul 11; 104(28): e43141. doi: 10.1097/MD.0000000000043141. PMID: 40660601; PMCID: PMC12263028.

28. Ding SW, Wang JJ. Diagnostic value and clinical significance of lncRNA LINC01123 combined with fibrinogen in acute cerebral infarction. Clin Neurol Neurosurg 2024 Jun; 241: 108309. doi: 10.1016/j.clineuro.2024.108309. Epub 2024 Apr 29. PMID: 38713963.

29. Hao H, Xing X, Li Y, Chu H, Zhao L, Cheng S, Liu Y, Wang T, Meng N, Duan R. Value evaluation of serum (sdLDLc*HCYc)/HDLc ratio in the stability of intracranial arterial plaques in patients with acute cerebral infarction. Acta Biochim Pol 2023 Dec 7; 70(4): 911–7. doi: 10.18388/abp.2020_6817. PMID: 38060820.

30. Lin X, Wang W, Tao T, Zhang D, Mao L, He X. Synthetic role of miR-411-5p and CT perfusion information in predicting clinical outcomes after thrombolysis in acute cerebral infarction. Acta Neurol Belg 2023 Apr; 123(2): 457–64. doi: 10.1007/s13760-022-02041-9. Epub 2022 Aug 6. PMID: 35933505.

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