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Predicting haemorrhagic transformation through serum biochemical indices for patients after endovascular treatment: a retrospective study

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ABSTRACT

Introduction. The aim of this study was to determine the serum biochemical markers that can predict the risk of haemorrhagic transformation (HT) before and after endovascular treatment (EVT).

Material and methods. This study included patients with anterior circulation large vessel occlusion (ACLVO) who underwent EVT within six hours of symptom onset between September 2017 and September 2022. These patients were retrospectively categorised into two groups: an HT group and a No-HT group.

Results. A total of 180 patients were included in the study, of whom 55 (30.6%) had HT. The monocyte count before EVT (p = = 0.005, OR = 0.694, 95% CI 0.536–0.898), the activated partial thromboplastin time before EVT (p = 0.009, OR = 0.186, 95% CI 0.699–0.952), and the eosinophil count after EVT (p = 0.038, OR = 0.001, 95% CI 0.000–0.018) were all found to be independent predictors of HT, with warning values of 6.65%, 22.95 seconds, and 0.035*10^^{9}/L, respectively. When compared to prediction using only demographic data [AUC = 0.662,95% CI (0.545, 0.780)], adding biochemical indices before EVT [AUC = 0.719,95% CI (0.617, 0.821)], adding biochemical indices after EVT [AUC = 0.670,95% CI (0.566, 0.773)], and adding both [AUC = 0.778,95% CI (0.686, 0.870)], the prediction efficiency of HT was improved among all three combinations, with no statistical significance.

Conclusions. The levels of serum biochemical markers were found to show significant changes before and after EVT in ACLVO patients. A combination of demographic data and serum biochemical markers proved to be effective in predicting the occurrence of HT in patients with ACLVO who underwent EVT.

Keywords: anterior circulation large vessel occlusion, endovascular treatment, haemorrhagic transformation, serum biochemical markers

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Introduction

In the Chinese population, stroke is the primary cause of death or disability, with the lifetime risk of stroke ranking the highest in the world [1]. The majority (c.70%) of stroke cases are attributed to acute ischaemic stroke (AIS) [1], of which anterior circulation large vessel occlusion (ACLVO) is the most prevalent type [2].

ACLVO involves vessel occlusion in the internal carotid artery (ICA), middle cerebral artery (MCA), or anterior cerebral artery (ACA) [3], and can result in more severe symptoms [4] and higher rates of disability or mortality [5] compared to other AIS subtypes.

ACLVO is associated with several risk factors such as hypertension, diabetes, hypercholesterolemia, smoking, and cerebral artery aneurysm [6–8]. These factors can contribute to cerebral artery narrowing, plaque buildup, and/or clot formation, leading to ACLVO [6–8]. Moreover, ACLVO is often caused by emboli originating from the heart or other arterial sources [6–8]. These emboli can travel through the bloodstream and block a large vessel in the brain, resulting in a stroke [6–8]. Therefore, ACLVO imposes a significant medical burden on individuals, families, and society.

The pathophysiology of ACLVO is mainly the obstruction of blood vessels, leading to local ischaemia and hypoxia of brain tissue, which can cause a series of physiological reactions such as brain cell death, brain oedema, and inflammatory response. These reactions can cause neurological dysfunction and damage to the nervous system, thereby affecting the patient's quality of life and prognosis [9].

The main treatment options for ACLVO currently are intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT). IVT is a reperfusion therapy used for treating acute ischaemic stroke. It involves delivering thrombolytic drugs to the entire body via intravenous injection or catheter, with the hope that the drugs can reach and dissolve the thrombus, restoring bloodflow. This therapy can effectively reverse neurological deficits, improve clinical outcomes, and prevent major disability after a stroke [10]. EVT involves the use of catheters and other devices inserted into blood vessels to remove the thrombus and restore bloodflow. EVT has been shown to be one of the most effective methods of treating ACLVO [11]. Experts worldwide recommend EVT for treating patients with early proximal anterior circulatory artery occlusion, based on five randomised trials conducted in 2015 which demonstrated the superiority of intravascular thrombectomy over standard care [12].

While EVT has been shown to significantly improve clinical outcomes in patients with early proximal anterior circulatory artery occlusion, it also poses a higher risk of haemorrhagic transformation (HT) than conventional therapy [13]. Many studies have explored the prognosis and treatment of ACLVO. These studies have mainly focused on prognosis evaluation, treatment methods, disease mechanisms, and other aspects. However, HT is a common complication in patients treated with EVT for ACLVO, and it may worsen the patient's prognosis. Although some studies have explored biomarkers for HT, there is currently no reliable biomarker that can predict HT after EVT [14]. HT, particularly symptomatic intracranial haemorrhage (SICH), is associated with a poor prognosis [15, 16] and poses greater challenges in terms of patient care. Therefore, early prediction of HT is vital.

Currently, the assessment of HT risk primarily relies on clinical status and neuroimaging [17]. Despite numerous studies on HT biomarkers, no serum indicators or biomarkers have yet been found that can effectively predict HT after EVT.

The aim of this study was to identify serum biochemical markers with predictive value for HT in ACLVO patients by comparing pre- and post-EVT levels.

Materials and methods

Study design

The Neurological Department at Chongqing University Three Gorges Hospital provided the data for our study, which was a retrospective review of data from an ongoing cohort. Informed consent was collected from every participant or their surrogate in accordance with the guidelines specified in the Declaration of Helsinki. The study protocols were reviewed and approved by the Clinical Trial Ethics Committee of our hospital (No. 20210185).

Participants

We recruited patients with acute ischaemic stroke (AIS) who underwent EVT at the Advanced Stroke Centre in Chongqing University Three Gorges Hospital, Wanzhou, China between September 2017 and September 2022 in this single-centre, retrospective, observational analysis. The inclusion criteria were: 1) imaging evidence of anterior circulation vascular occlusion (internal carotid artery, or anterior cerebral artery, or middle cerebral artery) upon admission; 2) maximum six hours from symptom onset to inguinal puncture; 3) Alberta Stroke Programme Early CT Score (ASPECTS) ≥ 6 before EVT; 4) imaging examinations such as CT or MR within 24 hours after EVT; and 5) serum biochemical examinations performed before, and within 24 hours after, EVT.

The exclusion criteria were: 1) intracranial parenchymal haemorrhage, ventricular system haemorrhage, or subarachnoid haemorrhage detected on admission CT or MR examination; 2) posterior circulation occlusion; 3) lack of required biochemical data before and after EVT; 4) heart, liver, lung, kidney, or other organ failure; 5) coagulation mechanism disorder or haemorrhagic disease; 6) allergy to contrast agent; 7) inability to undergo EVT; and 8) rapid progression to deep coma or death after EVT. A flow diagram outlining patient eligibility is presented in Figure 1.

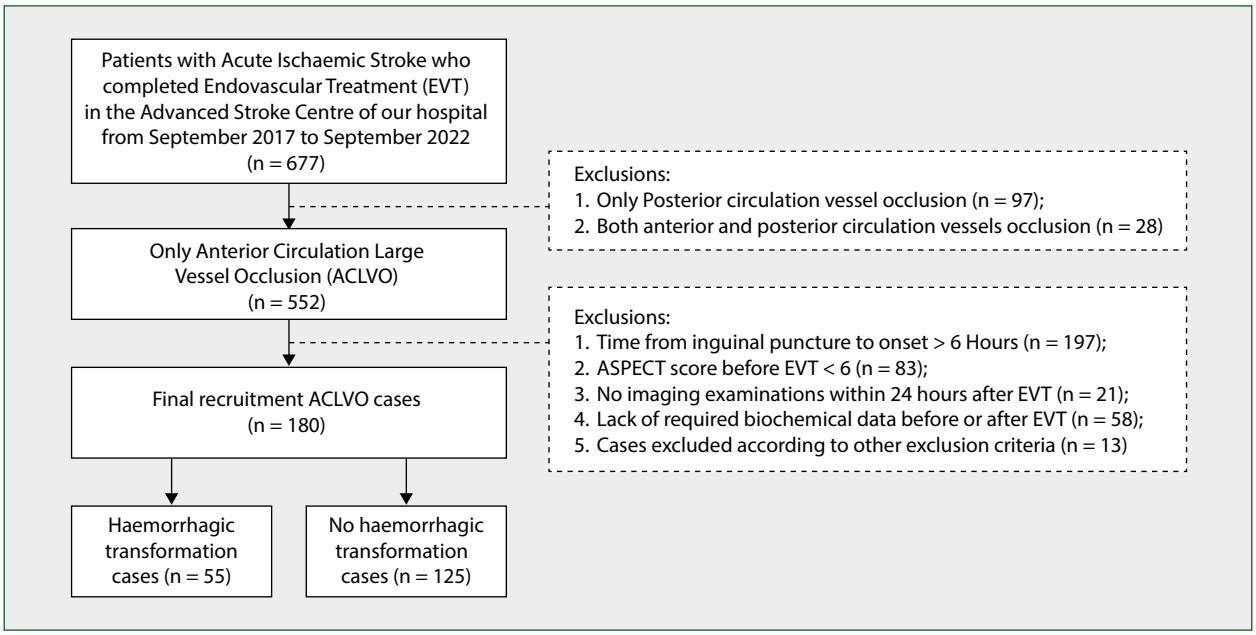

Figure 1. Flow diagram outlining patient eligibility

Data collection

Demographic characteristics such as sex, age, height, weight, and medical history (including hypertension, diabetes, atrial fibrillation, smoking, and alcohol consumption), were recorded.

The clinical data comprised surgical information (time from symptom onset to inguinal puncture, EVT duration, thrombectomy frequency of IVT, collateral circulation status, recanalisation condition), TOAST classification, ASPECT score, admission blood glucose and blood pressure (systolic and diastolic), admission GCS score, and admission NIHSS score.

The serum biochemical evaluations included an assessment of 25 parameters in routine blood tests, which encompassed White Blood Cells (WBC), Neutrophil Count (NEUT%), Lymphocyte Count (LYM%), Monocyte Count (MONO%), Eosinophil Count (EOS%), Basophilic Granulocytes Count (BASO%), Neutrophil Number (NEUT), Lymphocyte Number (LYM), Monocyte Number (MONO), Eosinophil Number (EOS), Basophilic Granulocytes Number (BASO), Red Blood Cell (RBC), Haemoglobin (Hb), Haematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Hb (MCH), Mean Corpuscular Hb Concentration (MCHC), Red Cell Volume Distribution Width CY (RDW-CY), Red Cell Volume Distribution Width SD (RDW-SD), Platelet (PLT), Plateletcrit (PCT), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Large Platelet Count (P-LCR), and C-reactive Protein (CRP).

Ten indices, which included serum potassium, sodium, chlorine, calcium, carbon dioxide (CO_2), urea, creatinine, glucose, estimated glomerular filtration rate (eGFR), and anion gap (AG), were assessed in the biochemical tests. A liver function test evaluated total protein (TP), albumin (ALB), globulin (GLB), albumin/globulin ratio (A/G), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transpeptidase (γ-GT), alkaline phosphatase (AKP), lactate dehydrogenase (LDH), and total bile acid (TBA). Prothrombin time (PT), international normalised ratio (PT-INR), prothrombin time activity (PTA), activated partial thromboplastin time (APTT), fibrinogen (FIB), thrombin time (TT), D-dimer, fibrin degradation products (FDPs), and antithrombin (AT) were measured in the coagulation function tests.

The biochemical indicators after EVT were obtained by drawing blood in the operating room after surgery. At that time, all patients underwent angiographic evaluation, and no bleeding was observed. Therefore, we ensured that there was no bleeding conversion in patients when blood was drawn after EVT. However, catheter angiography, while detailed, may miss small haemorrhagic infarctions due to resolution limits, contrast agent limitations, operator skill variations, and individual patient factors. Normal results post-procedure do not guarantee the absence of HT [18, 19]. After a 24-hour non-contrast CT scan, the persistence of contrast medium in the capillaries of the ischaemic territory or hyperperfusion in this area is often observed, which may be interpreted as HT. This can be distinguished by performing a non-contrast CT scan the next day [20, 21].

Imaging evaluation

The ASITN/SIR collateral circulation evaluation system, proposed by the American Society of Interventional

and Therapeutic Neuroradiology/Society of Interventional Radiology in 2003, was used to assess collateral circulation based on digital subtraction angiography (DSA) [22]. This system categorises collateral circulation into two groups: good collateral circulation (ASITN/SIR Level 0–2) or poor collateral circulation (ASITN/SIR Level 3–4).

Recanalisation status was assessed using the modified thrombolysis in cerebral infarction (mTICI) scale [23].

HT was defined as the occurrence of intracranial haemorrhage (either haemorrhagic secondary haemorrhage inside and outside the infarction area or vascular embolisation distribution area based on cerebral infarction [24] after EVT. According to the European Cooperative Acute Stroke Study-II (ECASS II) classifications [25], HT was subdivided into haemorrhagic infarction (HI) including HI1 or HI2 or parenchymal haemorrhage (PH) including PH1 or PH2.

Symptomatic intracranial haemorrhage (SICH) was diagnosed when a new intracranial haemorrhage was associated with any of the following: (1) an increase in NIHSS score by > 4 points compared to that immediately before the worsening; (2) an increase in NIHSS score by > 2 points in one category; or (3) deterioration of neurological status leading to intubation, hemicraniectomy, external ventricular drain placement, or other major medical or surgical intervention [26]. Two neuroradiologists evaluated all imaging examinations in a blinded manner, and in cases of disagreement, a third expert made the final decision.

Statistical analysis

The $\chi 2$ test was used to calculate categorical variables, and the Kolmogorov

Smirnov test was employed to evaluate the normality of the distribution of continuous variables. Student's t-test was applied for independent samples, while the Mann-Whitney U test was used for non-normally distributed data. Data was expressed as either mean ± standard deviation, median [quartile range (IQR)], or percentage. Firstly, we conducted a comparison of all serum biochemical indices before and after EVT in the subjects included in the study. All patients included had undergone mechanical thrombectomy and achieved a modified Thrombolysis in Cerebral Infarction (mTICI) grade 2b or 3. Subsequently, we compared all data, including demographic, clinical, and serum biochemical indices, between the HT (haemorrhagic transformation) group and the no-HT group. For the analysis of the outcome variable, i.e. haemorrhagic transformation, we initially performed a univariate correlation analysis. We selected variables with a p-value less than 0.05 from the univariate analysis and then proceeded with a multivariate analysis. To assess the independent risk factors for HT, we performed a binary multivariate regression analysis. Finally, we created four models to predict HT.

In Model A, the variables included were gender, smoking history, diabetes, collateral circulation status, time from onset to admission, body weight, and NIHSS score at hospital admission. Model B incorporated additional variables, namely monocyte ratio, activated partial thromboplastin time, D-dimer, and FDP quantification, into the variables present in Model A. Model C expanded the variables further by including eosinophil ratio, eosinophil count, erythrocyte distribution width CY, platelet distribution density, and direct bilirubin, again in addition to the variables from Model A. Model D encompassed the most extensive set of variables, adding eosinophil ratio, eosinophil count, erythrocyte distribution width CY, platelet distribution density, direct bilirubin, preoperative monocyte ratio, preoperative activation fraction, D-dimer, and preoperative FDP quantification to the variables in Model A. We plotted the receiver operating characteristic (ROC) curve and the precision-recall (PR) curve and compared the area under the curve (AUC) values of the four models [27]. The determination of cut-off values was achieved through logistic regression analysis, wherein the influence of predictive factors on the outcome variable was assessed. A ROC curve was constructed to evaluate the model's discriminatory performance, and the AUC was computed. Subsequently, we calculated the predictive sensitivity and specificity across varying values of the predictive factor and derived the Youden index. Cut-off value was identified as the predictive factor value that maximised the Youden index. This methodology enables the identification of an optimal cut-off value for the predictive factor, balancing sensitivity and specificity in predictive modelling. Statistical analysis was performed using SPSS 22.0, and P-values < 0.05 were considered statistically significant.

Results

Demographic data

In this study, we enrolled 180 patients with ACLVO, with a median age of 71.5 years (IQR = 14 years). Of these patients, 101 (56.1%) were male and 79 (43.9%) were female. The most common TOAST types were cardiogenic embolism (90 patients, 50%) and atherosclerosis (75 patients, 41.7%). Collateral circulation was rated as good in 104 patients (57.8%) and poor in 76 patients (42.2%). A total of 112 patients underwent EVT alone, while 68 patients underwent bridging therapy (EVT plus IVT). The mean time from symptom onset to inguinal puncture was 190.81 ± 88.28 minutes, the mean thrombectomy frequency was 1.91 ± 1.12 times, and the mean duration of EVT was 107.47 ± 75.89 minutes.

In this comprehensive research investigation encompassing two distinct cohorts, No-HT (N = 125) and HT (N = 55), our primary focus was to analyse and classify cerebral haemorrhages using the ECASS II criteria, specifically including Haemorrhage Infarction 1 (HI1), Haemorrhage Infarction 2 (HI2), Parenchymal Haemorrhage 1 (PH1), and Parenchymal Haemorrhage 2 (PH2). The data reveals distinctive patterns in the distribution of these haemorrhage types within each group. For the No-HT group, Parenchymal Haemorrhage

1 (PH1) emerged as the most prevalent, constituting 38.2% of cases, followed by Haemorrhage Infarction 2 (HI2) at 23.6%. Haemorrhage Infarction 1 (HI1) accounted for 12.7% of cases. Non-symptomatic intracranial haemorrhage was prevalent, comprising 61.8% of cases, while symptomatic intracranial haemorrhage (SICH) occurred in 38.2% of instances. Conversely, the HT group displayed a different profile of haemorrhage classifications. Parenchymal Haemorrhage 2 (PH2) was notably predominant, representing 52.4% of cases, followed by Haemorrhage Infarction 2 (HI2) and Haemorrhage Infarction 1 (HI1) in 19.0% and 14.3% of cases, respectively. Symptomatic intracranial haemorrhage (SICH) occurred in 14.3% of cases.

Serum biochemical indices before and after EVT

Table 1 presents a comparison of the serum biochemical indices between 180 ACLVO patients before EVT. Among the 25 blood routine examination indices, Monocyte Count (MONO%) exhibited a significant difference ($p = 0.006$, –2.756), indicating a potential association with HT. Additionally, Lymphocyte Count (LYM%) showed a trend towards significance ($p = 0.121$, –1.550). In terms of red blood cell and haemoglobin parameters, Mean Corpuscular Haemoglobin (MCH) and Haematocrit (Hct) did not show significant differences. Platelet parameters revealed non-significant variations in Mean Platelet Volume (MPV) and Platelet Count (PLT). Among the biochemical indices, Glomerular Filtration Rate (GFR) displayed a trend towards significance ($p = 0.099$, –1.649), while Serum Urea did not show a significant difference. In liver function, Lactate Dehydrogenase (LDH) and Total Bilirubin (TBIL) exhibited non-significant differences. Notably, coagulation function indices such as Activated Partial Thromboplastin Time (APTT), D-Dimer, and Fibrin Degradation Products (FDP) displayed significant differences ($p < 0.05$), suggesting potential implications for coagulation status in HT individuals before EVT.

These findings underline the nuanced associations between HT conditions and various biochemical parameters, providing valuable insights for clinical consideration.

Table 2 presents a comprehensive comparison of serum biochemical indices between cases with and without HT after EVT, encompassing 180 individuals. Notable observations emerged from the analysis of 25 blood routine examination indices. Eosinophil Count (EOS%) exhibited a significant decrease in HT cases compared to No-HT cases ($p = 0.010$, –2.578), signifying a potential influence of HT on this parameter post-EVT. Red Cell Volume Distribution Width CY (RDW-CY%) also displayed a significant difference ($p = 0.048$, –1.978), indicating potential alterations in red blood cell distribution in the HT group. Platelet Distribution Width (PDW%) demonstrated a significant increase in HT cases ($p = 0.018$, 2.359), suggesting potential variations in platelet size distribution. Additionally, serum glucose levels showed a trend towards significance ($p = 0.071$, 1.804), emphasising potential metabolic differences post-EVT. Coagulation function indices revealed notable changes, with Activated Partial Thromboplastin Time (APTT) showing a significant decrease in HT cases ($p = 0.062$, –1.864), and Antithrombin (AT%) displaying a significant increase in HT cases ($p = 0.161$,

Table 1. Comparison of serum biochemical indices between HT and No-HT cases before EVT

Total N = 180 before EVT	No-HT (N = 125), N(%)/ /median (IQR)	HT (N = 55), N(%)/ /median (IQR)	P-value	t/U
Blood routine examination, 25 indices				
White blood cells, WBC (*109/L)	7.67 (3.40)	7.65 (3.78)	0.533	0.623
Neutrophil count, NEUT% (%)	72.10 (20.70)	77.30 (17.57)	0.069	1.818
Lymphocyte count, LYM% (%)	21.10 (17.75)	16.15 (15.35)	0.121	–1.550
Monocyte count, MONO% (%)	5.60 (2.60)	4.90 (2.65)	0.006	–2.756
Eosinophil count, EOS% (%)	1.30 (1.65)	1.05 (1.90)	0.345	–0.945
Basophilic granulocytes count, BASO% (%)	0.40 (0.30)	0.30 (0.30)	0.907	–0.117
Neutrophil number, NEUT (*109/L)	5.53 (3.48)	5.74 (4.08)	0.296	1.045
Lymphocyte number, LYM (*109/L)	1.41 (1.04)	1.26 (1.04)	0.309	–1.018
Monocyte number, MONO (*109/L)	0.42 (0.25)	0.36 (0.17)	0.093	–1.681
Eosinophil number, EOS (*109/L)	0.09 (0.13)	0.09 (0.16)	0.406	–0.830
Basophilic granulocytes number, BASO (*109/L)	0.03 (0.01)	0.03 (0.02)	0.302	1.033
Red blood cell, RBC (*1012/L)	4.39 (0.71)	4.35 (0.81)	0.782	–0.277
Haemoglobin, Hb (g/L)	138 (24.50)	133 (22.25)	0.500	–0.675
Haematocrit, Hct (%)	41 (5.75)	40.50 (10.62)	0.540	–0.613
Mean corpuscular volume, MCV (fL)	92.80 (5.60)	94.10 (7.63)	0.765	0.299
Mean corpuscular haemoglobin, MCH (pg)	30.90 (2.15)	30.75 (2.13)	0.992	0.010

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Table 1 cont. Comparison of serum biochemical indices between HT and No-HT cases before EVT

Total N = 180 before EVT	No-HT (N = 125), N(%)/ /median (IQR)	HT (N = 55), N(%)/ /median (IQR)	P-value	t/U
Mean corpuscular haemoglobin concentration, MCHC (g/L)	330 (13.50)	331 (14.50)	0.676	0.417
Red cell volume distribution width CY, RDW-CY (%)	42.30 (31)	14.20 (30.85)	0.180	–1.340
Red cell volume distribution width SD, RDW-SD (%)	13.20 (1.10)	13.10 (0.90)	0.941	0.073
Platelet, PLT (*109/L)	188 (76)	160 (84.75)	0.173	–1.362
Plateletcrit, PCT	0.19 (0.07)	0.19 (0.07)	0.494	–0.684
Mean platelet volume, MPV (fL)	10.60 (1.75)	10.80 (2.95)	0.136	1.492
Platelet distribution width, PDW (%)	16.20 (0.45)	16.30 (0.55)	0.311	1.013
Large platelet count, P-LCR (%)	29.80 (11.60)	32.35 (20.50)	0.139	1.479
C-reactive protein, CRP (mg/L)	2.30 (4.20)	1.60 (2.26)	0.085	–1.725
Biochemical, 10 indices				
Serum potassium (mmol/L)	3.93 (0.49)	3.89 (0.61)	0.866	0.169
Serum sodium (mmol/L)	140 (4)	141 (5)	0.265	1.115
Serum chlorine (mmol/L)	105 (5.50)	104.35 (5.75)	0.988	0.015
Serum calcium (mmol/L)	2.26 (0.16)	2.25 (0.12)	0.486	–0.697
Serum carbon dioxide, CO_2 (mmol/L)	23.40 (3.85)	23.10 (3.25)	0.947	0.066
Serum urea (mmol/L)	5.70 (2.65)	6.10 (1.75)	0.613	0.506
Serum creatinine (µmol/L)	80 (23.50)	77.50 (31.75)	0.520	–0.643
Serum glucose (mmol/L)	6.35 (2.15)	6.54 (2.42)	0.755	0.312
Glomerular filtration rate, GFR (mL/min)	78.35 (28.85)	68.60 (23.60)	0.099	–1.649
Anion gap, AG	12.20 (4.65)	12.05 (3.28)	0.673	0.422
Liver function, 13 indices				
Total protein, TP (g/L)	67 (8.10)	66.30 (7.80)	0.843	–0.197
Albumin, ALB (g/L)	42.25 (4.13)	42.10 (4.60)	0.862	0.174
Globulin, GLB (g/L)	25.05 (6.75)	25.30 (6.30)	0.576	–0.559
Ratio of albumin and globulin, A/G	1.68 (0.43)	1.73 (0.53)	0.494	0.685
Total bilirubin, TBIL (µmol/L)	9.80 (7.02)	9.80 (7.10)	0.555	0.590
Direct bilirubin, DBIL (µmol/L)	3.90 (2.22)	4.30 (2.70)	0.680	0.413
Indirect bilirubin, IBIL (µmol/L)	5.25 (4.35)	6.20 (4)	0.375	0.887
Alanine aminotransferase, ALT (U/L)	15.65 (13.40)	16.70 (9)	0.784	0.274
Aspartate aminotransferase, AST (U/L)	21.95 (8.83)	22 (7.10)	0.410	0.823
γ-glutamyl transpeptidase,γ-GT (U/L)	24 (24.25)	28 (27.00)	0.933	–0.085
Alkaline phosphatase, AKP (U/L)	80 (31)	77 (14)	0.622	–0.492
Lactate dehydrogenase, LDH (U/L)	203 (80)	207 (65)	0.384	0.871
Total bile acid, TBA (µmol/L)	4.30 (5.65)	5.70 (9.05)	0.561	0.581
Coagulation function, 8 indices				
Prothrombin time, PT (seconds)	10.90 (1.20)	10.70 (1.10)	0.208	–1.258
International normalised ratio, PT-INR	0.95 (0.11)	0.93 (0.10)	0.096	–1.665
Prothrombin time activity, PTA (%)	109 (25.50)	114.40 (22.20)	0.176	1.354
Activated partial thromboplastin time, APTT (seconds)	24.80 (2.90)	24 (4.10)	0.013	–2.484
Fibrinogen, FIB (g/L)	2.90 (0.96)	2.89 (1.17)	0.650	–0.454
Thrombin time, TT (seconds)	17.90 (1.20)	17.60 (1.40)	0.731	–0.344
D-dimer (mg/L)	0.67 (0.87)	1.02 (1.71)	0.038	2.073
Fibrin degradation products, FDP (mg/L)	1.47 (2.13)	2.60 (3.30)	0.022	2.296
Antithrombin, AT (%)	87.50 (17.88)	86.25 (18.25)	0.807	–0.244

Student's t-test or Mann-Whitney U test between groups. Data expressed as median [quartile range (IQR)]; *p < 0.05; EVT — endovascular treatment

Table 2. Comparison of serum biochemical indices between HT and No-HT cases after EVT

Total N = 180 after EVT	No-HT (N = 125), N(%)/ /median (IQR)	HT (N = 55), N(%)/ /median (IQR)	P-value	t/U
Blood routine examination, 25 indices				
White blood cells, WBC (*109/L)	9.77 (5.16)	10.74 (5.93)	0.360	0.916
Neutrophil count, NEUT% (%)	83.30 (12.85)	85.60 (8.85)	0.227	1.208
Lymphocyte count, LYM% (%)	9.80 (7.90)	8.50 (7.80)	0.184	–1.328
Monocyte count, MONO% (%)	5.70 (3.10)	5.15 (3.25)	0.718	–0.362
Eosinophil count, EOS% (%)	0.20 (0.70)	0.00 (0.20)	0.010	–2.578
Basophilic granulocytes count, BASO% (%)	0.20 (0.20)	0.10 (0.20)	0.166	–1.385
Neutrophil number, NEUT (*109/L)	8.01 (4.91)	9.02 (5.09)	0.211	1.252
Lymphocyte number, LYM (*109/L)	1.07 (0.60)	0.91 (0.60)	0.315	–1.005
Monocyte number, MONO (*109/L)	0.52 (0.43)	0.52 (0.47)	0.606	0.516
Eosinophil number, EOS (*109/L)	0.01 (0.07)	0.01 (0.02)	0.010	–2.573
Basophilic granulocytes number, BASO (*109/L)	0.02 (0.02)	0.01 (0.02)	0.278	–1.085
Red blood cell, RBC (*1012/L)	3.91 (0.64)	3.95 (0.75)	0.856	0.182
Haemoglobin, Hb (g/L)	121 (22.50)	121.50 (21.50)	0.935	0.082
Haematocrit, Hct (%)	36.80 (6.50)	36.85 (6.08)	0.672	0.423
Mean corpuscular volume, MCV (fL)	93.80 (6)	94.35 (6.68)	0.341	0.952
Mean corpuscular haemoglobin, MCH (pg)	30.80 (1.90)	31.15 (2.20)	0.705	0.379
Mean corpuscular haemoglobin concentration, MCHC (g/L)	328 (11.00)	328 (9.50)	0.606	–0.516
Red cell volume distribution width CY, RDW-CY (%)	41.30 (31.35)	14.20 (30.35)	0.048	–1.978
Red cell volume distribution width SD, RDW-SD (%)	13.20 (0.88)	13.10 (0.83)	0.796	–0.259
Platelet, PLT (*109/L)	170 (72)	168 (64.25)	0.312	–1.011
Plateletcrit, PCT	0.18 (0.06)	0.18 (0.05)	0.601	–0.523
Mean platelet volume, MPV (fL)	10.80 (2.15)	11.10 (1.53)	0.206	1.265
Platelet distribution width, PDW (%)	16.10 (0.50)	16.30 (0.60)	0.018	2.359
Large platelet count, P-LCR (%)	30.20 (16.30)	33.60 (11.05)	0.202	1.276
C-reactive protein, CRP (mg/L)	12.70 (28.53)	9.05 (14.92)	0.396	–0.849
Biochemical, 10 indices				
Serum potassium (mmol/L)	3.95 (0.68)	3.92 (0.61)	0.303	–1.030
Serum sodium (mmol/L)	140 (3)	140 (7)	0.809	–0.242
Serum chlorine (mmol/L)	106 (3)	104 (7.50)	0.075	–1.778
Serum calcium (mmol/L)	2.12 (0.13)	2.11 (0.19)	0.830	0.215
Serum carbon dioxide, CO_2 (mmol/L)	22.20 (3.65)	22.70 (3.40)	0.618	0.499
Serum urea (mmol/L)	5.65 (2.50)	5.70 (3.18)	0.772	–0.289
Serum creatinine (µmol/L)	74 (26.00)	74 (27.50)	0.333	–0.967
Serum glucose (mmol/L)	6.99 (3.06)	7.63 (2.67)	0.071	1.804
Glomerular filtration rate, GFR (mL/min)	82.10 (24.08)	82.20 (27.70)	0.854	–0.184
Anion gap, AG	11.35 (4.28)	12.70 (5.18)	0.204	1.271
Liver function, 13 indices				
Total protein, TP (g/L)	60.30 (7.38)	59.30 (12.55)	0.858	0.179
Albumin, ALB (g/L)	36.95 (4.63)	37.20 (5.18)	0.471	0.721
Globulin, GLB (g/L)	22.75 (4.45)	21.95 (7.18)	0.954	–0.058
Ratio of albumin and globulin, A/G	1.63 (0.34)	1.63 (0.48)	0.741	0.330
Total bilirubin, TBIL (µmol/L)	11.70 (6.58)	12.55 (7.98)	0.083	1.734
Direct bilirubin, DBIL (µmol/L)	5.10 (2.55)	6.50 (3.38)	0.050	1.963
Indirect bilirubin, IBIL (µmol/L)	6.40 (3.85)	7.25 (4.65)	0.110	1.597

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Table 2 cont. Comparison of serum biochemical indices between HT and No-HT cases after EVT

Total N = 180 after EVT	No-HT (N = 125), N(%)/ /median (IQR)	HT (N = 55), N(%)/ /median (IQR)	P-value	t/U
Alanine aminotransferase, ALT (U/L)	14 (11.35)	16.55 (9.28)	0.219	1.228
Aspartate aminotransferase, AST (U/L)	23.50 (13.90)	23.60 (15.10)	0.760	0.306
γ-glutamyl transpeptidase,γ-GT (U/L)	22.50 (21.25)	31 (31.25)	0.271	1.102
Alkaline phosphatase, AKP (U/L)	67.50 (24.50)	66 (30.25)	0.421	–0.804
Lactate dehydrogenase, LDH (U/L)	210 (100.25)	239.50 (117.00)	0.057	1.903
Total bile acid, TBA (μmol/L)	3.05 (5.30)	3 (4.90)	0.544	–0.607
Coagulation function, 8 indices				
Prothrombin time, PT (seconds)	11.40 (1.75)	11.20 (1.70)	0.210	–1.254
International normalised ratio, PT-INR	1.03 (0.17)	0.97 (0.18)	0.099	–1.648
Prothrombin time activity, PTA (%)	93.90 (28.45)	102.50 (21.40)	0.111	1.593
Activated partial thromboplastin time, APTT (seconds)	26.20 (4.95)	25.20 (4.90)	0.062	–1.864
Fibrinogen, FIB (g/L)	2.71 (2.06)	2.85 (1.24)	0.903	0.122
Thrombin time, TT (seconds)	17.50 (2.90)	17.60 (1.50)	0.788	–0.269
D-dimer (mg/L)	2.47 (3.97)	2.56 (6.32)	0.375	0.887
Fibrin degradation products, FDP (mg/L)	6.45 (8.38)	5.80 (13.20)	0.518	0.647
Antithrombin, AT (%)	76.05 (19.45)	89.60 (23.93)	0.161	1.400

Student's t-test or Mann-Whitney U test between groups. Data expressed as median [quartile range (IQR)]; *p < 0.05; EVT — endovascular treatment

1.400). These findings shed light on post-EVT biochemical alterations associated with HT, offering valuable insights for further clinical consideration.

Demographic data between No-HT and HT patients

Table 3 shows demographic data for HT and No-HT patients, revealing significant differences between the two groups in terms of male gender, history of smoking, history of diabetes, collateral circulation status, time from symptom onset to inguinal puncture, weight, and admission NIHSS score ($p < 0.05$). Additionally, before EVT, significant differences were observed in several serum biochemical indexes, including monocyte count, APTT, D-dimer, and FDP ($p < 0.05$). The examination of treatment modalities revealed that 64% of patients in the No-HT group underwent only EVT, while the corresponding percentage in the HT group was 58.2%. The distribution of treatments between the two groups did not reach statistical significance ($p = 0.458$). Additionally, 36% of patients in the No-HT group received EVT combined with IVT (EVT+IVT), compared to 41.8% in the HT group. For patients receiving only EVT, the odds ratio (OR) in the HT group relative to the No-HT group was 1.278. This table provides a comprehensive overview of the differences in treatment types and distribution between the two patient groups, offering an initial comparison of treatment strategies. After EVT, significant differences were found in Eosinophil Count, Eosinophil Number, Red Cell Volume Distribution Width CY, Platelet Distribution Width, and DBIL ($p < 0.05$).

Multivariate regression analysis of HT

Table 4 presents the results of multivariate analysis indicating that several factors are independent risk factors for HT. These include poor collateral circulation status (adjusted $p = 0.022$, adjusted odds ratio [OR] = 2.228, confidence interval [CI]: 1.121–4.428), time from symptom onset to inguinal puncture (adjusted $p = 0.047$, adjusted OR = 1.040, 95% CI: 1.000–1.082, cutoff value = 242.5 minutes), NIHSS score on admission (adjusted $p = 0.044$, adjusted OR = 1.058, 95% CI: 1.002–1.117, cut-off value = 16.5 points), monocyte count and MONO% (%) before EVT (adjusted $p = 0.005$, adjusted OR = 0.694, 95% CI: 0.536–0.898, cut-off value = 6.65%), APTT before EVT (adjusted $p = 0.009$, adjusted OR = 0.886, 95% CI: 0.699–0.952, cut-off value = 22.95 seconds), and eosinophil number and EOS after EVT (adjusted $p = 0.038$, adjusted OR = 0.002, 95% CI: 0.001–0.018, cut-off value = 0.035* 109/L).

Prediction models for HT

We created four HT prediction models and used the AUC to assess each model's performance. 0.662 (95% CI: 0.545–0.780), 0.719 (95% CI: 0.617–0.821), 0.670 (95% CI: 0.566–0.773), and 0.778 (95% CI: 0.686–0.870) were the AUC values for models A, B, C, and D, respectively. The AUC values of the four models showed no statistically significant differences ($p > 0.05$). Model D had the highest AUC value and the precision-recall (PR) curve indicated good overall accuracy. Model C had the least accurate performance, as indicated by its position in the middle of the PR curve. Figure 2 and Table 5 set out all the results.

Table 3. Clinical characteristics and risk factors associated with haemorrhagic transformation in acute ischaemic stroke patients undergoing endovascular treatment

			No-HT (N = 125), N(%)/median (IQR)	HT (N = 55), N(%)/ /median (IQR)	P-value	OR/U
Classification of haemorrhage, ECASS II		Haemorrhage infarction 1, HI1		7 (12.7%)	NA	
		Haemorrhage infarction 2, HI2		13 (23.6%)		
		Parenchymal Haemorrhage 1, PH1		21 (38.2%)		
		Parenchymal Haemorrhage 2, PH2		14 (25.5%)		
Non-symptomatic intracranial haemorrhage				34 (61.8%)	NA	
Symptomatic intracranial haemorrhage, SICH				21 (38.2%)	NA	
Classification of haemorrhage, ECASS II		Haemorrhage infarction 1, HI1		3 (14.3%)	NA	
		Haemorrhage infarction 2, HI2		4 (19.0%)		
		Parenchymal Haemorrhage 1, PH1		3 (14.3%)		
		Parenchymal Haemorrhage 2, PH2		11 (52.4%)		
Gender		Male	77 (61.6%)	24 (43.6%)	0.025*	2.072
		Female	48 (38.4%)	31 (56.4%)		
History	Smoking	1	45 (36.0%)	11 (20.0%)	0.033*	0.444
		0	80 (64.0%)	44 (80.0%)		
	Alcohol consumption	1	33 (26.4%)	14 (25.5%)	0.894	0.952
		0	92 (73.6%)	41 (74.5%)		
	Hypertension	1	63 (50.4%)	28 (50.9%)	0.950	1.021
		0	62 (49.6%)	27 (49.1%)		
	Diabetes	1	7 (5.6%)	8 (14.5%)	0.045*	2.869
		0	118 (94.4%)	47 (85.5%)		
	Atrial fibrillation	1	61 (48.8%)	27 (49.1%)	0.971	1.012
		0	64 (51.2%)	28 (50.9%)		
Collateral circulation status, ASITN/SIR		Good	79 (63.2%)	25 (45.5%)	0.026*	0.485
		Poor	46 (36.8%)	30 (54.5%)		
Treatment	Only EVT		80 (64%)	32 (58.2%)	0.458	1.278
	EVT+IVT		45 (36%)	23 (41.8%)		
TOAST classification	Large-artery atherosclerosis		54 (43.2%)	21 (38.2%)	0.078	–1.762
	Cardioembolism		58 (46.4%)	32 (58.2%)		
	Small-artery occlusion		1 (0.8%)	0 (0%)		
	Stroke of other determined aetiology		5 (4.0%)	1 (1.8%)		
	Stroke of undetermined aetiology		7 (5.6%)	1 (1.8%)		
mTICI after EVT	3		104 (83.2%)	45 (81.8%)	0.831	0.214
	2b		2 (1.6%)	0 (0%)		
	2c		16 (12.8%)	10 (18.2%)		
	Others or Failure		3 (2.4%)	0 (0%)		
Age, years			72 (14.00)	70 (13)	0.647	0.458
Time from symptom onset to inguinal puncture, minutes			180 (120.00)	193.00 (170)	0.026*	2.231
ASPECT score before EVT			9 (3)	8 (3)	0.118	–1.562
Admission blood glucose, mmol/L			6.70 (2.10)	7.20 (3)	0.310	1.014
Height, cm			162 (15)	160 (15)	0.159	–1.410
Weight, kg			63 (15)	60 (11)	0.019*	–2.345

→

Table 3 cont. Clinical characteristics and risk factors associated with haemorrhagic transformation in acute ischaemic stroke patients undergoing endovascular treatment

		No-HT (N = 125), N(%)/median (IQR)	HT (N = 55), N(%)/ median (IQR)	P-value	OR/U
Systolic blood pressure, mmHg		139 (37.50)	142 (44)	0.373	0.891
Diastolic blood pressure, mmHg		81 (23)	78 (31)	0.963	–0.047
Admission GCS score		11 (6)	10 (6)	0.078	–1.762
Admission NIHSS score		14 (9)	17 (9)	0.023*	2.265
Times of thrombectomy		2 (1)	2 (2)	0.980	–0.025
Duration of EVT, minutes		90 (80)	90 (50)	0.921	0.099
Serum biochemical examinations					
Before EVT	Monocyte Count, MONO% (%)	5.60 (2.60)	4.90 (2.65)	0.006*	–2.756
	Activated Partial Thromboplastin Time, APTT (seconds)	24.80 (2.90)	24.00 (4.10)	0.013*	–2.484
	D-Dimer (mg/L)	0.67 (0.87)	1.02 (1.71)	0.038*	2.073
	Fibrin Degradation Products, FDP (mg/L)	1.47 (2.13)	2.60 (3.30)	0.022*	2.296
After EVT	Eosinophil Count, EOS% (%)	0.20 (0.70)	0.00 (0.20)	0.010*	–2.573
	Eosinophil Number, EOS (*109/L)	0.01 (0.07)	0.01 (0.02)	0.010*	-2.573
	Red Cell Volume Distribution Width CY, RDW-CY (%)	41.30 (31.35)	14.20 (30.35)	0.048*	-1.978
	Platelet Distribution Width, PDW (%)	16.10 (0.50)	16.30 (0.60)	0.018*	2.359
	Direct Bilirubin, DBIL (μmol/L)	5.10 (2.55)	6.50 (3.38)	0.049*	1.963

χ2 test and Mann-Whitney U test between groups. Data expressed as mean ± standard deviation or numbers (percentages); *p < 0.05; OR — odds ratio; HT — haemorrhagic transformation; ECASS II — European Co-operative Acute Stroke Study-II; ASITNSIR — American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; EVT — endovascular treatment; IVT — intravenous thrombolysis; TOAST — trial of org 10172 in acute stroke treatment; mTICI — modified thrombolysis in cerebral infarction; ASPECT — Alberta Stroke Programme Early CT Score

Table 4. Multivariate regression analysis of HT

Indicator	P-value	OR	95%CI		Cut-off value
			Lower	Upper	
Collateral circulation status	0.022	2.228	1.121	4.428	Poor
Time from symptom onset to inguinal puncture	0.047	1.040	1.000	1.082	242.5 minutes
NIHSS score on admission	0.044	1.058	1.002	1.117	16.5 points
MONO% before EVT	0.005	0.694	0.536	0.898	6.65%
APTT before EVT	0.009	0.886	0.699	0.952	22.95 seconds
EOS after EVT	0.038	0.002	0.001	0.018	0.035*109/L

MONO% — monocyte count (%); APTT — activated partial thromboplastin time; EOS — eosinophil number; OR — odds ratio; CI — confidence interval

Discussion

Our study found that the rate of HT was 30.6%, while the incidence of symptomatic intracranial haemorrhage (SICH) was 18.9%. These findings are consistent with previous studies, which reported HT rates ranging from 7.5% to 49.5% and SICH rates ranging from 0.6% to 20% depending on the type and timing of EVT [28, 29]. Our study adds to the existing body of literature, and supports the need for continued research and improvement in the prevention and management of HT in patients undergoing EVT for acute ischaemic stroke.

Numerous clinical factors have been associated with HT. In terms of patient demographic data, previous studies have identified older age, hypertension, and hyperglycaemia as potential risk factors for HT [30–33]. As patients age, their physical functions decline, and they may develop various underlying diseases such as hypertension and diabetes, which can lead to microvascular degeneration, decreased vascular elasticity, and vascular wall damage, all of which may increase the risk of HT [30, 31]. In addition, some preclinical studies using animal stroke models [34, 35] have shown that increasing age and hyperglycaemia are closely related to HT.

The second factor associated with HT is the timing of EVT. Delayed initiation of EVT has been found to increase the risk of HT, possibly due to oxidative stress response and blood-brain barrier dysfunction [36].

Thirdly, poor collateral circulation has consistently been linked to a higher risk of HT in previous studies [28, 37, 38]. In patients with poor collateral circulation, the blood supply to the ischaemic focus mainly relies on developing tertiary collateral circulation. Under conditions of high perfusion pressure, these newly formed collateral vessels increase local

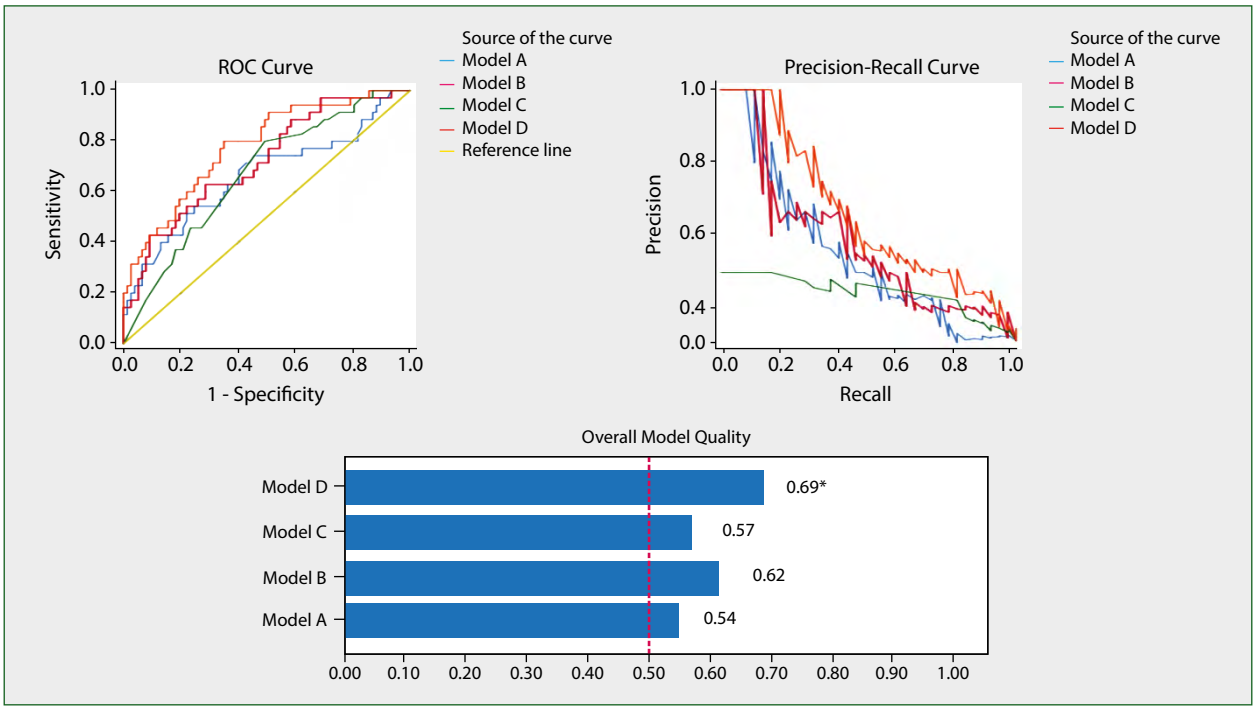

Figure 2. Receiver Operating Characteristic (ROC) curves and Precision-Recall (PR) curves and Overall Quality of four models. Model A: Only demographic and clinical data included as predictors; Model B: On basis of model A, serum biochemical indices before EVT were included; Model C: On basis of model A, serum biochemical indices after EVT were included; Model D: On basis of model A, serum biochemical indices both before and after EVT were included. AUC value of Model D is highest, and PR curve shows good overall accuracy. PR curve shows the least accurate to be Model C, which is located in middle of graph. *A good model has a value above 0.5. A value of less than 0.5 indicates model is no better than random prediction. Use caution in interpreting this chart because it only reflects a general measure of overall model quality. Model quality can be considered 'good' even if correct prediction rate for positive responses does not meet specified minimum probability. Use classification table to examine correct prediction rates

Table 5. Values of area under curve (AUC) and paired-sample area difference under receiver operating characteristic (ROC) curves

Test result Variable(s)	AUC or difference	Std. Error or Std. Error difference[a]	Asymptomatic Sig.[b] or Sig. (2-tail)[c]	Asymptomatic 95% confidence interval	
				Lower bound	Upper bound
Model A	0.662	0.060	0.007	0.545	0.780
Model B	0.719	0.052	0.000	0.617	0.821
Model C	0.670	0.053	0.001	0.566	0.773
Model D	0.778	0.047	0.000	0.686	0.870
Model A–Model B	–0.057	0.333	0.436	–0.199	0.086
Model A–Model C	–0.007	0.332	0.901	–0.125	0.110
Model A–Model D	–0.116	0.326	0.108	–0.257	0.025
Model B–Model C	0.049	0.324	0.518	–0.100	0.199
Model B–Model D	–0.059	0.308	0.058	–0.120	0.002
Model C–Model D	–0.108	0.314	0.083	–0.231	0.014

Test result variable(s): model A, model C has at least one tie between positive actual state group and negative actual state group. Statistics may be biased; a — under nonparametric assumption; b — null hypothesis: true area = 0.5; c — null hypothesis: true area difference = 0

osmotic pressure, thereby increasing the risk of HT [37, 38]. Additionally, high NIHSS scores, particularly on admission, have also been found to be associated with HT [39, 40]. Furthermore, some studies have shown that long-term smoking and alcohol consumption not only increase the risk of cardiovascular disease, particularly stroke [41], but also increase the risk of HT in stroke patients [42].

Our study confirmed that poor clinical collateral circulation, longer time from symptom onset to inguinal puncture, and higher NIHSS score on admission were independent risk factors for HT. This is consistent with previous research. Therefore, clinical diagnosis, treatment, and monitoring of high-risk groups should be strengthened. We also observed significant changes in 31/54 serum biochemical indices before and after EVT, probably

due to disease progression and EVT. Furthermore, monocyte count before EVT, ATPP before EVT, and eosinophil number after EVT were identified as independent predictors of HT, highlighting the importance of timely monitoring.

Studies have increasingly highlighted that after stroke, HT results from damage to the blood–brain barrier due to the inflammatory response [34]. Monocytes, an essential part of innate immunity, play a crucial role in regulating proinflammatory and anti-inflammatory processes [43]. A study evaluated the time course and phenotypes of monocyte subtypes in 46 consecutive stroke patients and 13 age-matched controls. It was found that certain subtypes of monocytes were associated with detrimental effects, such as increased mortality and early clinical deterioration following a stroke. On the other hand, rare subsets of monocytes can promote tissue repair and angiogenesis [44]. Furthermore, preclinical studies suggest that monocytes/macrophages can prevent HT in mice [45]. Recent research has identified the monocyte/high-density lipoprotein cholesterol (MHR) count as a new prognostic marker of cardiovascular disease, combining proinflammatory and anti-inflammatory processes [46]. Low MHR values are independently linked to an increased risk of HT and symptomatic HT in AIS patients [47]. Nevertheless, the involvement of monocytes in HT in humans remains limited. Our study confirmed that monocytes are associated with HT. Abrupt changes in monocyte counts before EVT may reflect an early inflammatory response and an elevated risk of HT.

Previous studies have extensively demonstrated that the coagulation and fibrinolytic system undergoes dynamic activation and rapid changes in the early stages of AIS, and these changes are implicated in the development of HT [17, 48]. Platelets, fibrin monomer complex (FMX), thrombin-activated fibrinolysis inhibitors (TAFI), plasminogen-activated fibrinolysis inhibitors (PAFI), endogenous thrombin potential (ETP), and peak thrombin are clinical biomarkers that reflect the function of coagulation and have been linked to a high risk of HT in AIS patients receiving IVT or EVT [49]. However, according to some research [40, 50], there is no correlation between some of these markers and HT. In a study of AIS patients who did not receive recanalisation therapy (thrombolysis or intravascular therapy), Chen et al. [51] measured coagulation function indicators within 24 hours of admission, and discovered that prolonged TT was independently associated with spontaneous HT, whereas PT, APTT, INR, and FIB were not.

We discovered in our study that APTT was independently associated with HT. APTT is a coagulation function indicator that reflects the activity of coagulation factors in the early first stage, especially of the endogenous coagulation pathway [52].

The immune system response after AIS can have both protective and damaging effects on nerve tissue [53]. Previous studies have suggested that high levels of eosinophils may indicate an increased risk of AIS [54]. It has also been observed that a decrease in eosinophil levels is associated with a higher risk of short-term death and infection after AIS, as well as more severe limb dysfunction [55]. However, the role of normal eosinophil levels in AIS is still not fully understood. Wang et al. [56] conducted a study on 300 AIS patients without high eosinophil syndrome (HES) and found that eosinophil count and percentage were effective predictors of survival during hospitalisation. Jucevičiūtė et al. [57] found that higher levels of eosinophil absolute count (AEC) were associated with a lower risk of HT in AIS patients treated with intravenous RTPA. In our study, we found that serum eosinophil count was an independent risk factor for HT, with a critical level below 0.035*109/L, which was consistent with previous studies indicating low eosinophil levels [50]. A decrease in eosinophil levels reflects high stress in the body and indicates the potential for inflammation and infection, which can lead to HT.

Our study did not find associations between HT and several serum biochemical parameters previously reported in other studies, including ALB [58], uric acid [59], serum calcium [60], homocysteine [61], serum magnesium [62], AKP [63], RBC distribution width [64], neutrophils [65], lymphocytes [66], TBA [67], AST, or ALT [68]. For the four predictive models, while there were slight differences in their AUCs, none of these differences showed statistical significance. This suggests that, in the sample population studied, adding or removing predictive indicators did not lead to significant changes in the outcomes of the models.

Several factors contributed to these results. Firstly, the limited sample size is likely to have played a role. Increasing the sample size might amplify such differences and achieve statistical significance. Secondly, some biochemical indicators did not exhibit significant changes between pre-operation and post-operation, which affected the predictive efficacy when considering them separately. Additionally, certain biochemical markers experienced varying degrees of changes with disease progression and haemorrhagic transformation, necessitating dynamic monitoring in future research to provide a more objective reflection of the results.

Limitations of this study

Our study has several limitations. Firstly, it was conducted at a single centre with a small sample size and over a long timespan, which could limit the generalisability of our findings. Secondly, blood lipid-related indicators were not included in our analysis due to the absence of lipid tests before and after EVT for many patients. Previous studies have reported associations between blood lipid levels, the use of lipid-lowering drugs, and haemorrhagic transformation [29, 40, 69]. Thirdly, our definition of haemorrhagic transformation relied on imaging examination within 24 hours after EVT, thus potentially missing patients with delayed HT. Moreover, due to the limited sample size, we did not perform TOAST classification-AIS subtyping analysis, which would be beneficial for observing trends of AIS subtypes. Finally, there may be other imaging techniques that could provide more accurate or detailed information about HT. Further research could

explore the use of other imaging techniques to assess HT and compare their effectiveness against that of non-contrast CT [70]. Additionally, the timeframe of 24 hours may not be optimal for all patients, and future studies could investigate the optimal timing for HT assessment. Notably, the relatively short duration of blood sample collection (107.47 ± 75.89 minutes) impedes a comprehensive observation of the actual trends in blood variables. Factors such as the administration of anaesthesia during the procedure may influence the obtained blood samples, introducing potential confounding variables. This constraint is acknowledged as one of the study's limitations, and we intend to address it explicitly in the limitations section of our manuscript.

It is important for readers to be mindful of these constraints when interpreting the study's conclusions. Future studies should aim to increase the sample size to facilitate such observations. Lastly, we did not investigate the medication history of patients before or after admission, which could influence some serum biochemical parameters.

Conclusions

The serum biochemical markers showed significant changes before and after EVT in ACLVO patients. The combination of demographic data and these markers proved effective in predicting HT, thereby highlighting the importance of timely detection of biochemical indicators. However, the prediction models had similar efficiency, indicating the need for a larger multicentre prospective study. Furthermore, the different independent predictors of HT before and after EVT suggest distinct physiological mechanisms at different stages of stroke. Further research is required to identify valuable biomarkers or indicators for postoperative management of EVT in AIS patients.

Article information

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Consent for publication: *Not applicable.*

Conflicts of interest: *The authors declare no competing interests.*

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