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Effect of intravenous thrombolysis in acute ischemic stroke patients with cerebral microbleeds and analysis of risk factors for hemorrhagic transformation

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Abstract. – OBJECTIVE: To investigate the safety and efficacy of intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) in patients with acute ischemic stroke (AIS) and cerebral microbleeds (CMBs) and analyze the risk factors for hemorrhagic transformation (HT).

PATIENTS AND METHODS: The clinical data of 220 patients with CMB within the first 4.5 h after the onset of acute ischemic stroke treated in our hospital from September 2018 to December 2019 were retrospectively analyzed. Then, these patients were evenly assigned into two groups based on whether the intravenous thrombolysis with rt-PA was adopted or not. Next, the neurological deficit was scored using the National Institute of Health stroke scale (NIHSS) before and after treatment, the modified Rankin scale (mRs) score of patients was recorded at 90 d after treatment, and the incidence rate and death rate of intracranial hemorrhage (ICH) after treatment were recorded and evaluated. Additionally, the univariate and logistic regression analyses were employed for the risk factors for HT in patients after thrombolysis.

RESULTS: The NIHSS score declined to (7.08±3.75) points and (7.83±4.22) points at 24 h after treatment and (3.67±3.63) points and (4.92±3.87) points at 7 d after treatment, respectively, in Thrombolysis group and Control group, which were significantly lower than those before treatment ($p<0.05$). The NIHSS score displayed no statistically significant difference between the two groups at 24 h after treatment ($p=0.165$), whereas it was markedly lower in Thrombolysis group than that in Control group at 7 d after treatment ($p=0.015$). At 90 d after treatment, there were 98 (89.1%) and 79 (71.8%) cases of good prognosis in Thrombolysis group and Control group, respectively, and the difference was statistically significant between the two groups ($p=0.002$). Besides, the number of patients with SICH and aSICH was 3 and 2 (2.7% *vs*. 1.8%, $p=0.651$) and 9 and 4 (8.2% *vs*. 3.6%, $p=0.152$) in Thrombolysis group and Control group, respectively, and the number of deaths was 7 and 5 (6.4% *vs*. 4.5%, $p=0.553$) in the two groups, showing no statistically significant difference. The results of univariate and multivariate analyses revealed that the time from stroke onset to thrombolysis, baseline NIHSS score, and history of atrial fibrillation were independent risk factors affecting the HT of patients undergoing intravenous thrombolysis [odds ratio (OR) =1.330, 95% confidence interval (95% CI) =1.079-1.851, $p=0.019$; OR=1.592, 95% CI=1.025-2.767, $p=0.010$; OR=2.428, 95% CI=1.814-3.643, $p=0.016$].

CONCLUSIONS: Compared with those undergoing no intravenous thrombolysis with rt-PA, patients with acute ischemic stroke and CMB who received intravenous thrombolysis with rt-PA exhibit significantly improved short-term neurological function recovery and long-term prognosis, but the incidence and mortality rates of ICH have no statistically significant differences. Moreover, the time from stroke onset to thrombolysis, baseline NIHSS score, and history of atrial fibrillation are independent risk factors affecting the HT of patients treated with intravenous thrombolysis.

Key Words:
Cerebral microbleeds, Intravenous thrombolysis, Ischemic stroke, Hemorrhagic transformation.

Abbreviations

rt-PA: recombinant tissue plasminogen activator; CMB: cerebral microbleed; HT: hemorrhagic transformation; NIHSS: National Institute of Health stroke scale; mRs: modified Rankin scale; ICH: intracranial hemorrhage;

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tPA: tissue plasminogen activator; MRI: magnetic resonance imaging; DWI: diffusion-weighted imaging; NINDS: National Institute of Neurological Disorders and Stroke; SICH: symptomatic ICH; aSICH: asymptomatic ICH; SPSS: Statistical Product and Service Solutions; TOAST: Trial of ORG 10172 in Acute Stroke Treatment; ECASS III: European Cooperative Acute Stroke Study III; VISTA: Virtual International Stroke Trials Archive.

Introduction

In the case of acute ischemic stroke (AIS), revascularization is applied to interfere with the arterial occlusion, so as to restore cerebral blood flow and improve neurological prognosis. Clinically, intravenous tissue plasminogen activator (tPA) is mostly used[1,2]. In the treatment of acute ischemic stroke, intravenous thrombolysis continuously improves the neurological prognosis of patients, but it can also increase the risk of hemorrhagic transformation (HT)[3]. HT refers to the hemorrhage occurring in ischemic foci after stroke, whose incidence rate is 10-40% in ischemic stroke patients treated with thrombolytic therapy[4]. Identifying patients with high risk of bleeding through early detection can reduce the risk of intracranial hemorrhage (ICH) after thrombolysis.

Cerebral microbleed (CMB) is a subclinical lesion caused by the leakage of blood through the damaged wall of microvessels, characterized by hemosiderin deposition in the brain parenchyma. It has been reported that the microbleeds shown on the image are a risk factor for ICH after intravenous thrombolysis. However, various studies[5,6] have shown that ICH after intravenous thrombolysis has no correlation with the microbleeds shown on the image. It is still debatable whether CMB increases the risk of ICH and whether these patients receive thrombolytic therapy. This study aims to explore the safety and efficacy of recombinant tPA (rt-PA) intravenous thrombolysis in patients with acute ischemic stroke and CMB and analyze the risk factors for HT.

Patients and Methods

Patients

The clinical data of 220 patients with CMB within the first 4.5 h after the onset of acute ischemic stroke treated in our hospital from September 2018 to December 2019 were retrospectively analyzed. Then, these patients were evenly assigned into two groups based on whether the intravenous thrombolysis with rt-PA was adopted or not. The thrombolytic therapy was conducted for patients based on the 2013 AHA/ASA Guidelines for the Early Management of Patients with Acute Ischemic Stroke and the 2014 Chinese Guidelines for Acute Ischemic Stroke Management. All patients underwent magnetic resonance imaging (MRI) [T2*, T1, T2, and diffusion-weighted imaging (DWI) sequences] scans. DWI and T2 sequences were used to assess the location of ischemic lesions, and T2*-weighted GRE sequence was utilized to evaluate the location of CMB and early HT. The inclusion criteria were set as follows: 1) patients with ischemic stroke and obvious neurological dysfunction, 2) those with first onset, 3) those with the onset time <4.5 h, and 4) those aged ≥18 years old. The exclusion criteria involved (1) patients with past history of cerebral hemorrhage, (2) those with intracranial injuries (such as head traumas and fractures) with high possibility of hemorrhage in the past 3 months, (3) those with past history of clear or suspected subarachnoid hemorrhage, (4) those suffering from intracranial diseases with high risk of hemorrhage, including brain tumors, aneurysms or vascular malformations, (5) those recently receiving intracranial or intraspinal surgery, (6) those who could not receive MRI examination due to various reasons (such as claustrophobia and pacemaker insertion), (7) those with severe heart, liver, and kidney dysfunction or obvious mental disorders, or (8) those with severe blood coagulation disorder and bleeding tendency. Among the 220 patients, there were 132 males and 88 females aged 33-79 years old, with an average of (61.63±9.69) years old. The baseline data of patients showed no statistically significant differences between the two groups, which were comparable (Table I, $p>0.05$). All patients enrolled were informed of this study and signed the informed consent in accordance with Declaration of Helsinki. This study was approved by the Ethics Committee of The Second Hospital of Shanxi Medical University.

Therapeutic Methods

In Thrombolysis group, patients were treated with intravenous thrombolysis with alteplase (trade name: Actilyse) within 4.5 h after onset at a dose of 0. 9 mg/kg, and the maximum dose

Table I. Baseline characteristics of the studied patients.

Parameters	Thrombolysis group n = 110	Control group n = 110	*p*-value
Age (years)	62.19 ± 9.73	60.84 ± 9.57	0.301
Gender (Male/ Female)	69/41	63/47	0.492
Mean time since stroke onset (h)	3.68 ± 1.28	3.45 ± 1.31	0.189
TOAST type (n, %)			0.621
Large artery atherosclerosis	57 (51.8%)	59 (53.6%)	
Small artery occlusion	30 (27.3%)	27 (24.5%)	
Cardioembolism	17 (15.5%)	15 (13.6%)	
Others	6 (5.5%)	9 (8.2%)	
Baseline NIHSS score	8.76 ± 4.29	9.08 ± 4.41	0.486
Baseline systolic pressure (mmHg)	154 ± 20	157 ± 22	0.291
Baseline blood glucose (mmol/L)	7.3 ± 2.9	7.7 ± 3.1	0.324
Smoking history (n, %)	64 (58.2%)	69 (62.7%)	0.491
Diabetes mellitus history (n, %)	27 (24.5%)	34 (30.9%)	0.292
Hypertension history (n, %)	52 (47.3%)	60 (54.5%)	0.281
Coronary heart disease history (n, %)	16 (14.5%)	23 (20.9%)	0.217
Hyperlipidemia history (n, %)	59 (53.6%)	67 (60.9%)	0.276
Atrial fibrillation history (n, %)	6 (5.5%)	11 (10.0%)	0.207
TIA history (n, %)	5 (4.5%)	9 (8.2%)	0.269

Notes: NIHSS: National Institutes of Health stroke scale; TIA: Transient Ischemic Attacks.

was ≤90 mg. 10% of the total dose was injected intravenously within 1 min, and the remaining was intravenously instilled within 1 h. Then, further supportive treatments with brain protection agents, lipid-regulating drugs, and plaque-stabilizing drugs were carried out to improve cerebral circulation and metabolism, and other underlying diseases were treated. All patients received head MRI (T1, T2, DWI, and T2*GRE), MRA, and PWI examinations at 24 h after thrombolytic therapy. If there was no bleeding on images, antiplatelet aggregation therapy was performed by oral administration of 100 mg of aspirin and 75 mg of clopidogrel.

In Control group, patients were given antiplatelet drugs at the same dose as well as the same basic symptomatic treatments.

Observation Indexes

The diagnostic criteria for intracranial microhemorrhage[7] included (1) there are circular or quasi-circular uniform-density low signals on T2*GRE sequence or SWI sequence, with clear edges, (2) it is paramagnetic and contains blood degrading components, (3) there is blooming effect, (4) the diameter is 5-10 mm, (5) at least one-half is surrounded by the brain parenchyma, (6) there is no T1 or T2-weighted high signal (such as cavernous hemangioma, tumor, and hemorrhagic infarction), (7) there is no diffuse axonal injury, and (8) there are no others low signals. The microbleeds were classified into the following three levels as per the Miembleed Anatomical Rating Scale (MARS): no microbleeds (n=0), a small amount of microbleeds (n=1-2), and multiple microbleeds (n≥3)[8].

Based on the evaluation criteria of the National Institute of Neurological Disorders and Stroke (NINDS) clinical trials, a decrease of ≥4 points in the National Institute of Health stroke scale (NIHSS) score of patients and an evident improvement in the neurological deficit at 24 h and 7 d after thrombolytic therapy indicated good short-term prognosis, while a decrease of <4 points in the NIHSS score of patients at 24 h and 7 d after thrombolytic therapy suggested poor short-term prognosis[9]. Patients were followed up for prognosis after 3 months. A modified Rankin scale (mRS) score of 0-2 points evaluated at 3 months after treatment was considered as good long-term prognosis, prompting that patients can live and work independently, whereas a mRS score of 3-6 points evaluated at 3 months after treatment was defined as poor long-term prognosis, indicating that stroke patients have neurological dysfunction, cannot live independently, and need family care.

The HT was compared between the two groups of patients. HT is divided into symptomatic ICH (SICH) and asymptomatic ICH (aSICH). SICH refers to the symptoms of HT in patients receiving intravenous thrombolysis according to

the classification standards of the NINDS, and aSICH means only signs of HT is found on head CT after intravenous thrombolytic therapy, without the symptoms of HT in patients[10,11]. Moreover, the risk factors for HT after intravenous thrombolytic therapy were analyzed in combination with related literature reports.

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 22.0 (IBM, Armonk, NY, USA) was utilized for statistical analysis. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and *t*-test was employed for the comparison between two groups and paired data within the group. Enumeration data were expressed as ratio (%), and χ^2-test or Fisher's exact test was used for comparison. Multivariate logistic regression analysis was adopted to analyze the risk factors of HT after intravenous thrombolysis. $p<0.05$ suggested that the difference was statistically significant.

Results

Comparison of Neurological Score Between the Two Groups of Patients Before and After Treatment

Before treatment, no statistically significant difference was found in the NIHSS score between the two groups ($p=0.486$). The NIHSS score was decreased to (7.08±3.75) points and (7.83±4.22) points at 24 h after treatment and (3.67±3.63) points and (4.92±3.87) points at 7 d after treatment, in Thrombolysis group and Control group, respectively, which were significantly lower than that before treatment ($p<0.05$). Besides, the NIHSS score displayed no statistically significant difference between the two groups at 24 h after treatment ($p=0.165$), whereas it was markedly lower in Thrombolysis group than that in Control group at 7 d after treatment ($p=0.015$) (Table II).

Comparisons of Efficacy and ICH V Between the Two Groups of Patients at 90 d After Treatment

At 90 d after treatment, there were 98 (89.1%) and 79 (71.8%) cases of good long-term prognosis in Thrombolysis group and Control group, respectively, and the difference was statistically significant between the two groups ($p=0.002$) (Table II). The number of patients with SICH and aSICH was 3 and 2 (2.7% *vs.* 1.8%, $p=0.0651$) and 9 and 4 (8.2% *vs.* 3.6%, $p=0.152$) in Thrombolysis group and Control group, respectively, and the number of deaths was 7 and 5 (6.4% *vs.* 4.5%, $p=0.553$) in the two groups, displaying no statistically significant differences (Table II).

Univariate and Multivariate Analyses on HT of Patients Undergoing Intravenous Thrombolysis

Patients in Thrombolysis group were divided into HT group (n=12) and non-HT group (n=98) based on the incidence of HT. Then, the age, gender, time from stroke onset to thrombolysis, TOAST (*Trial of ORG 10172 in Acute Stroke Treatment*) class, baseline NIHSS score, baseline systolic blood pressure, baseline diastolic blood pressure, baseline blood glucose level, baseline

Table II. Comparison of NIHSS score, mRS scores and prognosis indexes of patients in the two groups.

Parameters	Thrombolysis group n = 110	Control group n = 110	*p*-value
NIHSS score			
Pretreatment	8.76 ± 4.29	9.08 ± 4.41	0.486
24 hs Posttreatment	7.08 ± 3.75	7.83 ± 4.22	0.165
7 days Posttreatment	3.67 ± 3.63	4.92 ± 3.87	0.015
90 days Posttreatment mRS (n, %)			0.002
0-2 points	98 (89.1%)	79 (71.8%)	
3-6 points	12 (10.9%)	31 (28.2%)	
Intracranial hemorrhage (n, %)			
SICH	3 (2.7%)	2 (1.8%)	0.651
aSICH	9 (8.2%)	4 (3.6%)	0.152
Death (n, %)	7 (6.4%)	5 (4.5%)	0.553

Notes: NIHSS: National Institutes of Health stroke scale; mRS: Modified Rankin scale; SICH: Symptomatic intracranial hemorrhage; aSICH: Asymptomatic intracranial hemorrhage.

Table III. Univariate analysis of hemorrhagic transformation after intravenous thrombolysis of the studied patients.

Parameters	HT n = 12	Non HT n = 98	*p*-value
Age (years)	65.57 ± 10.31	60.86 ± 9.83	0.122
Gender (Male)	6 (8.7%)	63 (91.3%)	0.334
Time from stroke onset to thrombolysis (h)	4.08 ± 1.58	3.30 ± 1.67	0.048
TOAST type (n, %)			0.372
Large artery atherosclerosis	9 (15.8%)	48 (84.2%)	
Small artery occlusion	2 (6.7%)	28 (93.3%)	
Cardioembolism	1 (5.9%)	16 (94.1%)	
Others	0 (0%)	6 (100%)	
Baseline NIHSS score (points)	14.58 ± 6.49	6.77 ± 4.84	0.001
Baseline systolic pressure (mmHg)	171 ± 24	151 ± 21	0.003
Baseline diastolic pressure (mmHg)	93 ± 18	86 ± 16	0.161
Baseline blood glucose (mmol/L)	8.8 ± 3.8	7.1 ± 3.2	0.092
Baseline Hb (g/L)	131.28 ± 31.58	137.30 ± 27.26	0.479
Baseline PLT (1012/L)	205.91 ± 45.65	214.34 ± 40.50	0.576
Baseline fibrinogen (g/L)	2.92 ± 1.12	3.19 ± 1.19	0.457
Smoking history (n, %)	6 (50.0%)	58 (59.2%)	0.553
Hypertension history (n, %)	9 (75.0%)	43 (43.9%)	0.001
Diabetes mellitus history (n, %)	4 (33.3%)	23 (23.5%)	0.484
Atrial fibrillation history (n, %)	4 (33.3%)	2 (2.0%)	0.001
Coronary heart disease history (n, %)	2 (16.7%)	14 (14.3%)	0.586
TIA history (n, %)	1 (8.3%)	4 (4.1%)	0.445
Hyperlipidemia history (n, %)	5 (41.7%)	54 (55.1%)	0.541

Notes: HT: Hemorrhagic transformation; NIHSS: National Institutes of Health stroke scale; TIA: Transient Ischemic Attacks.

Hb, baseline PLT, baseline fibrinogen, history of smoking, history of hypertension, history of diabetes mellitus, history of atrial fibrillation, history of coronary heart disease, history of TIA and history of hyperlipidemia were included in the univariate analysis of HT. The results uncovered that the time from stroke onset to thrombolysis, baseline NIHSS score, baseline systolic blood pressure, history of hypertension, and history of atrial fibrillation were risk factors for HT in patients receiving intravenous thrombolysis (p=0.048, p<0.001, p=0.003, p<0.001, p<0.001) (Table III).

Next, the factors of statistical differences in the univariate analysis were included in multivariate logistic regression analysis, and it was found that the time from stroke onset to thrombolysis, baseline NIHSS score, and history of atrial fibrillation were independent risk factors affecting the HT of patients undergoing intravenous thrombolysis [odds ratio (OR) =1.330, 95% confidence interval (95% CI)= 1.079-1.851, p=0.019, OR=1.592, 95% CI=1.025-2.767, p=0.010, OR=2.428, 95% CI=1.814-3.643, p=0.016] (Table IV).

Discussion

Currently, intravenous thrombolysis with rt-PA is one of the most effective approaches for the treatment of ischemic stroke. According to the results of European Cooperative Acute Stroke Study III (ECASS III) on thrombolysis (OR=1.26, 95% CI=1.05-1.51), the intravenous injection of

Table IV. Multivariable Cox Regression analysis of hemorrhagic transformation after intravenous thrombolysis of the studied patients.

Parameters	OR value	95% CI	*p*-value
Time from stroke onset to thrombolysis (h)	1.330	1.079-1.851	0.019
Baseline NIHSS score	1.592	1.025-2.767	0.010
Baseline systolic pressure (mmHg)	1.035	0.891-1.414	0.209
Hypertension history (n, %)	1.063	0.933-1.527	0.251
Atrial fibrillation history (n, %)	2.428	1.814-3.643	0.016

Notes: HT: OR: Odds Ratio; CI: Confidence interval; NIHSS: National Institutes of Health stroke scale.

rt-PA significantly enhances the efficacy and observably improves the 90-d clinical prognosis (the mRS score is 0 or 1) of patients receiving thrombolytic therapy within 3-4.5 h after the onset of AIS at the same time. Besides, the results of the Third International Stroke Trial (IST III) in 2012 where 3,035 patients with AIS were included reveal that the thrombolytic therapy is effective, and it also benefits patients aged over 80 years old at the same time[12,13]. At present, it is agreed in most international guidelines that the treatment with intravenous rt-PA within 4.5 h after onset is safe and effective for AIS patients. Based on the North American Stroke Registry, an advancement of 15 min in the starting time of the treatment suggests an increase of 4% in the good prognosis during hospitalization and a decrease of 4% in the risks of SICH and death[14]. In this study, it was found that the NIHSS score was prominently lower in Thrombolysis group than that in Control group (p=0.015), and the number of patients with good prognosis was considerably higher in Thrombolysis group than that in Control group [98 (89.1%) *vs.* 79 (71.8%), p=0.002].

Post-thrombolysis HT, especially ICH, is the major severe complication of intravenous thrombolysis. According to the comparison of the total occurrence rate of bleeding in stroke patients treated with and without thrombolytic therapy in NINDS research, the total occurrence rate of bleeding of the former is about 3 times that of the latter[15]. Based on ECASS III, the risk of symptomatic bleeding in patients treated with thrombolytic therapy is 10 times that of those not receiving thrombolytic therapy[16]. In this study, the results showed that the incidence rate of ICH after treatment was slightly higher in Thrombolysis group than that in Control group, but the difference was not statistically significant (p>0.05). The efficacy is often poor once SICH occurs, which is an important factor leading to an increase in the disability rate of patients and affecting the prognosis. For this reason, discovering the risk factors for post-thrombolysis HT is of important clinical significance.

The time from onset to thrombolysis is an important factor leading to post-thrombolysis bleeding events. The thrombolysis time window of alteplase stipulated by the NINDS is within 3 h, but the ECASS-III study results show that thrombolytic therapy with alteplase is still effective at 3-4.5 h after onset[17]. It is observed in the IST-3 that the risk of SICH rises by 6% in patients undergoing thrombolysis within 6 h after onset[18]. The window of intravenous thrombolysis with rt-PA is within 3 h in the United States, Canada, Croatia and Moldova, and 4.5 h in other countries. In China, different indications and contraindications are also formulated for patients undergoing thrombolysis at the time window of within 3 h, 3-4.5 h and within 6 h in thrombolysis guidelines. However, after satisfying various indications and exclusion principles, it is still discovered that the bleeding risk is higher in patients receiving thrombolysis within 3-6 h than that in those receiving thrombolysis within 3 h.

Besides, the pre-thrombolysis NIHSS score is proven to be an independent risk factor for post-thrombolysis bleeding. The occurrence rate of slCH after thrombolysis in patients with a baseline NIHSS score of 20 points is 11 times that of those with a NIHSS score of 5 points. A multi-center survey of acute stroke patients undergoing thrombolysis with rt-PA has shown that the NIHSS score is an independent risk factor for ICH, and an increase of 1 point in the NIHSS score indicates an increase of 1.38% in the risk of bleeding. Patients with NIHSS score <5 points will have a low risk of poor prognosis such as HT if they undergo intravenous thrombolysis with alteplase within 3-4.5 h[19]. The IST-3 shows that the efficacy of thrombolytic therapy in patients with atrial fibrillation is as good as that in those without atrial fibrillation. The results of the Virtual International Stroke Trials Archive (VISTA) are consistent with the findings of the IST-3 study[20]. However, it was found in a meta-analysis in 2016 uncovered that the occurrence rate of SICH in atrial fibrillation patients receiving thrombolytic therapy after ischemic stroke is increased, and the 90-d functional outcome is relatively poor[21]. Saposnik et al[22] also showed that the proportion of ICH in patients with ischemic stroke and atrial fibrillation after intravenous thrombolysis is increased, and the good prognosis rate after thrombolysis has no evident increase.

Moreover, hypertension is also confirmed in the research to be an independent risk factor for post-thrombolysis HT, and the systolic blood pressure is negatively correlated with stroke prognosis[23-25]. The blood pressure of 80% of patients with acute ischemic stroke will show a transient increase, and it will spontaneously decline in a short period of time, which is related to the stress response of the body and the physiological response to cerebral hypoxia and increased intracranial pressure. As required in the 2014 Chinese guidelines for the diagnosis and treatment of

ischemic stroke, the pre-thrombolysis systolic and diastolic blood pressures are controlled at <180 mmHg and <100 mmHg, respectively. The results of univariate and multivariate analyses in this study revealed that the time from stroke onset to thrombolysis, baseline NIHSS score, and history of atrial fibrillation were independent risk factors affecting the HT of patients treated with intravenous thrombolysis.

There are some limitations in this research. This study is a retrospective study with limited sample size, short follow-up period and incomprehensive follow-up content. In addition, the long-term prognosis of patients was not analyzed in this study. Hence, multicenter and large long-term follow-up studies are needed in the future to verify the conclusion of this study.

Conclusions

Compared with those undergoing no intravenous thrombolysis with rt-PA, patients with acute ischemic stroke and CMB who received intravenous thrombolysis with rt-PA exhibit significantly improved short-term neurological function recovery and long-term prognosis, but the incidence and mortality rates of ICH have no statistically significant differences. In addition, the time from stroke onset to thrombolysis, baseline NIHSS score, and history of atrial fibrillation are independent risk factors affecting the HT of patients treated with intravenous thrombolysis. The findings of this study provide a basis for the treatment of acute ischemic stroke and CMBs.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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