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Safety of alteplase intravenous thrombolysis and influencing factors of clinical outcome in elderly patients with acute ischemic stroke

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Abstract

Objective To explore the safety of intravenous thrombolysis with alteplase (rt-PA) in the treatment of acute ischemic stroke (AIS) in the elderly (≥ 80 years old) and with analyze the influencing factors of its clinical outcome.

Methods A total of 144 elderly patients (≥ 80 years old) with AIS who were admitted to our hospital from April 2018 to October 2019 were divided into the elderly thrombolytic group ($n = 55$) and the elderly non-thrombolytic group ($n = 89$) according to their different treatment methods, and 166 non-elderly AIS thrombolytic patients in the same period were selected as the non-elderly thrombolytic group. Routine antiplatelet therapy or anticoagulant therapy was given to the elderly non-thrombolytic group, while intravenous thrombolysis with rt-PA was given to the elderly thrombolytic group and the non-elderly thrombolytic group. The changes in National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS), and intracranial hemorrhage transformation within 7 days, mortality within 3 months were used to evaluate the prognosis and safety of patients in each group. Binary Logistic regression was used to analyze the independent factors affecting the long-term prognosis of thrombolytic therapy for AIS in the elderly.

Results After the treatment, the short-term prognosis and the long-term prognosis improvement rates in the non-elderly thrombolytic group and the elderly thrombolytic group were higher than that in the elderly non-thrombolytic group ($P < 0.05$). There was no statistical difference in mortality between the elderly thrombolytic group and the elderly non-thrombolytic group or in intracranial hemorrhage transformation among the different groups ($P > 0.05$). Binary logistic regression analysis showed that NIHSS score before treatment was an independent risk factor affecting the long-term prognosis of elderly AIS patients after thrombolysis ($P < 0.05$).

Conclusion Elderly AIS patients after rt-PA thrombolysis therapy can improve the short-term, long-term prognosis. The risk of intracranial hemorrhage transformation and death is not higher than that of elderly non thrombolytic patients, indicating that rt-PA treatment is safe for elderly AIS patients. The NIHSS score before treatment was an independent risk factor affecting the long-term prognosis of elderly AIS patients after thrombolytic therapy.

Keywords Acute ischemic stroke, Alteplase, Safety, Elderly, Influencing factors

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Introduction

In recent years, the incidence of stroke continues to rise, which has become one of the leading causes of death, of which acute ischemic stroke (AIS) is the most common stroke type [1]. After the occurrence of AIS, there is an ischemic penumbra between the normal brain tissue and the completely necrotic lesion. To restore the blood supply to the cells in this region as much as possible within 4.5 h and promote the survival of the incomplete necrotic brain tissue is the most effective way to reduce the disability and mortality rate of AIS [2, 3]. Conventional antiplatelet therapy has been proved to be effective in the past, but evidence-based medicine has confirmed that intravenous alteplase (rt-PA) thrombolysis is the most effective method for ultra-early treatment of AIS at present. However, the consequent safety problems such as secondary hemorrhage and reperfusion injury limit its application in elderly patients [4, 5]. However, the high disability and high mortality rate of AIS are more prominent in elderly patients. For elderly patients, only conventional antiplatelet or anticoagulant therapy is often ineffective. Although in various diagnosis and treatment guidelines related to AIS in recent years, age has not been taken as the exclusion criterion for the application of rt-PA intravenous thrombolysis, there are still many disputes on whether to apply rt-PA and thrombolytic therapy for elderly AIS patients, considering that elderly patients may be more likely to cause intracranial hemorrhage [6, 7]. Therefore, in this study, we compared the short-term and long-term prognosis differences and intracranial hemorrhage of different treatment measures in elderly and non-elderly AIS patients within the time window to determine whether elderly AIS patients can benefit from rt-PA and the safety of drug use and conducted a binary Logistic regression analysis to identify the independent factors affecting the long-term prognosis of AIS thrombolysis treatment in the elderly patients. The specific report is as follows.

Materials and methods

Research object

A total of 144 elderly AIS patients (aged≥80 years) who were admitted to our hospital from April 2018 to October 2019 were divided into the elderly thrombolytic group (n=55) and the elderly non-thrombolytic group (n=89) according to their treatment methods, and 166 non-elderly AIS thrombolytic patients in the same period were selected as the non-elderly thrombolytic group. Inclusion criteria: Patients who met the relevant diagnostic criteria of AIS [8], who were confirmed by cranial CT or MRI and excluded intracranial hemorrhage and had no imaging changes of early large-scale cerebral infarction; onset time<4.5 h. Exclusion criteria: The presence of subarachnoid hemorrhage; History of head trauma, cerebral infarction, myocardial infarction, etc. in the past three months; History of cerebral hemorrhage in the past; There is coagulation dysfunction; Blood glucose<2.7 mmol/L; The blood pressure was still higher than 180/105 mmHg after antihypertensive treatment; the infarct focus exceeds 1/3 of the MCA distribution area or the ASPECTS score is <5 points. There were 26 males and 29 females in the elderly thrombolysis group, and the average age was (84.40±3.54) years old. There were 36 males and 53 females in the elderly non-thrombolytic group, with an average age of (84.33±3.64) years old. There were 115 males and 51 females in the non-elderly thrombolytic group, with an average age of (65.36±11.00) years old. This study was approved by the Hospital Ethics Committee and the informed consent form was signed by the patient or his/her family members.

Research methods

Therapeutic method

All patients were given multifunctional monitoring, oxygen inhalation, establishment of bilateral venous channels, monitoring of patients' vital signs and controlling blood pressure, maintenance of water and electrolyte balance and other routine symptomatic treatment immediately after they were admitted and weighed.

The patients in the elderly non-thrombolytic group were treated with antiplatelet aggregation or anticoagulant therapy. Patients in the non-elderly thrombolytic group and the elderly thrombolytic group were given intravenous infusion of rt-PA (Boehringer Ingelheim, Germany, specification: 20 mg/piece and 50 mg/piece) according to their body weight at the dose of 0.9 mg/kg, with the polar amount of 90 mg. 10% of the total amount was statically pushed within 1 min from the start of medication, and the rest was completed within 1 h. A reexamination of the CT scan of the head after 24 h and, in the absence of bleeding, administration of antiplatelet aggregation or anticoagulation as well as routine treatment for ischemic stroke were performed.

Observation index

The NIHSS is used to evaluate the short-term prognosis and the NIHSS score on the seventh day is observed. Compared with before treatment, decreases in NIHSS score≥4 points or NIHSS scores of 0 and 1 were considered to improvement, fluctuations in NIHSS score within 3 points were considered to be no change, and increases in NIHSS score≥4 points or deaths were considered to worsen [9]. The modified Rankin scale (mRS) after three months was used to evaluate the long-term prognosis of the patients. The mRS score≤1 was classified as good long-term prognosis, while mRS scores 2–6 was classified as poor long-term prognosis [10]. Compare the 7-day

Table 1 Comparison of short-term prognosis among patients in each group(n,%)

Groups	Improvement	No change	Worsen	Improvement rate(%)
Elderly thrombolytic group($n=55$)	21	22	12	38.18
Elderly non-thrombolytic group($n=89$)	10	57	22	11.2*
Non-elderly thrombolytic group($n=166$)	93	55	18	56.02*#
χ^2 value				48.517
P value				0.000

Note: Compared with Elderly thrombolytic group, $^{*}P<0.05$; Compared with Elderly non-thrombolytic group, $^{\#}P<0.05$

intracranial hemorrhage transformation and 3-month mortality after thrombolysis, especially in elderly thrombolysis patients and elderly non-thrombolysis patients, to evaluate the safety of intravenous thrombolysis in elderly patients with acute ischemic stroke.

The elderly patients with thrombolysis were grouped based on long-term prognosis, and their clinical data were analyzed. Binary Logistic regression was used to analyze the independent factors affecting the long-term prognosis of elderly patients with AIS after thrombolytic therapy.

Statistical methods

The SPSS26.0 software was used for data processing. Measurement data were expressed as mean±standard deviation, and enumeration data were expressed as (%). *t*-test was used for pairwise comparison, and χ^2-test was used for enumeration data. Multivariate analysis was performed using a binary logistic regression model. The test level was $\alpha=0.05$, and $P<0.05$ indicated that the difference was statistically significant.

Results

Comparison of short-term prognosis among patients in each group

After the treatment, the short-term prognosis improvement rates in the non-elderly thrombolytic group and the elderly thrombolytic group were higher than that in the elderly non-thrombolytic group, and the improvement rate in the non-elderly thrombolytic group was higher than that in the elderly thrombolytic group, and the differences were statistically significant ($P<0.05$). See Table 1.

Table 2 Comparison of long-term prognosis of patients in each group(n, %)

Groups	Good prognosis	Poor prognosis	Good prognosis rate(%)
Elderly thrombolytic group($n=55$)	16	39	29.09
Elderly non-thrombolytic group($n=89$)	13	76	14.61*
Non-elderly thrombolytic group($n=166$)	98	68	59.04*#
χ^2 value			51.190
P value			0.000

Note: Compared with Elderly thrombolytic group, $^{*}P<0.05$; Compared with Elderly non-thrombolytic group, $^{\#}P<0.05$

Table 3 Intracranial hemorrhage transformation within 7 days and mortality within 3 months after thrombolysis in patients of each group(n,%)

Groups	Intracranial hemorrhage transformation rate	Mortality rate
Elderly thrombolytic group($n=55$)	8(14.55)	20(36.36)
Elderly non-thrombolytic group($n=89$)	14(15.73)	33(37.07)
Non-elderly thrombolytic group($n=166$)	28(16.87)	16(9.64)*#
χ^2 value	0.179	32.899
P value	0.914	0.000

Note: Compared with Elderly thrombolytic group, $^{*}P<0.05$; Compared with Elderly non-thrombolytic group, $^{\#}P<0.05$

Comparison of long-term prognosis of patients in each group

After treatment, the long-term good prognosis rates in the non-elderly thrombolytic group and the elderly thrombolytic group were higher than that in the elderly non-thrombolytic group, and the long-term good prognosis rate in the non-elderly thrombolytic group was higher than that in the elderly thrombolytic group, and the differences were statistically significant ($P<0.05$). See Table 2.

Intracranial hemorrhage transformation within 7 days and mortality within 3 months after thrombolysis in patients of each group

After the treatment, the mortality rates in the non-elderly thrombolytic group were lower than that in the elderly thrombolytic group and the elderly non-thrombolytic group, and the difference was statistically significant ($P<0.05$). There was no statistical difference in mortality between the elderly thrombolytic group and the elderly non-thrombolytic group or in intracranial hemorrhage transformation among the different groups ($P>0.05$). See Table 3.

Comparison of clinical data in elderly AIS patients with thrombolysis with different long-term prognosis

Univariate analysis showed that there were significant differences in D- dimer, NIHSS score before treatment and history of heart failure among elderly AIS patients with thrombolysis with different long-term prognosis ($P<0.05$). See Table 4.

Multivariate analysis of long-term prognosis of elderly patients with AIS after thrombolysis

Binary Logistic regression analysis was performed using NIHSS score before treatment, D- dimer, and history of heart failure was involved as independent variables. The results showed that NIHSS score before treatment was an independent risk factor affecting the long-term prognosis of elderly AIS patients after thrombolysis ($P<0.05$). See Tables 5 and 6.

Discussion

In many industrialized countries, advanced age is the fastest-growing age group. At this age, cerebrovascular disease is the leading cause of death and disability [11]. Acute ischemic stroke has become a clinically related life-threatening disease for the elderly, not only because of its increased incidence (one third of all patients with first ischemic stroke belong to this age group), but also because of poor prognosis, related dysfunction, dementia and the risk of recurrence in stroke, as well as high global and social burden. Compared to younger patients, elderly patients with ischemic or hemorrhagic stroke have poorer short-term prognosis, higher in-hospital mortality rates, and a lower proportion of asymptomatic patients upon discharge [12]. In China, we have entered the elderly society, and with the decrease in birth rate, there are more and more elderly people, especially those over 80 years old. As age increases, the incidence of acute ischemic stroke also increases, with many complications and severe conditions, such as neurological deficits that cannot be well recovered, which can bring serious burdens to families and society.

After the occurrence of AIS, the blood flow of the ischemic tissue in the penumbra was still higher than the cell failure threshold, and the neurons were still in the survival state, which could last for 4–8 h. Therefore, timely and effective thrombolytic therapy, saving the ischemic penumbra, restoring blood perfusion, and reducing the infarct size were the key to improve the prognosis of AIS. Alteplase (rt-PA) is currently one of the most widely used thrombolytic drugs in clinical practice, and it can act on thrombotic fibrin, accelerate local microcirculation, and promote neurological functional recovery. The thrombolytic effect is far superior to conventional antiplatelet therapy, and it is also the only drug supported by evidence-based medicine and approved for intravenous thrombolysis in acute ischemic stroke [13–15]. However, there is still controversy about its application in elderly AIS patients. Although it has been reported that the risk of bleeding after intravenous thrombolysis in elderly patients is significantly higher than that in non-elderly patients [4], it has also been reported recently [16–18] that intravenous thrombolysis with rt-PA does not increase the probability of hemorrhage, poor prognosis and death in elderly patients after thrombolysis.

NIHSS scores the degree of neurological dysfunction from 11 items such as disturbance of consciousness and eye movement, which is one of the commonly used scales for clinical evaluation of neurological recovery in AIS patients, while mRS is a commonly used scale for clinical evaluation of patients' ability to live, which can better reflect the impact of AIS on patients' ability to live [19, 20]. In this study, the NIHSS changes were used as the short-term prognosis evaluation index of AIS, and the mRS score was used as the long-term prognosis evaluation index of AIS. The results showed that after treatment, the short-term and long-term prognosis of non-elderly thrombolytic group and elderly thrombolytic group were better than that of the elderly non-thrombolytic group; the short-term and long-term prognosis of non-elderly thrombolytic group were better than that of elderly thrombolytic group. This indicates that the benefit of intravenous thrombolysis with rt-PA in elderly patients is decreased to a certain extent compared with that in non-elderly people, but it is still significantly superior to conventional treatment. In addition, the results of this study also showed that the mortality rates in the non-elderly thrombolytic group were lower than those in the elderly thrombolytic group and the elderly non-thrombolytic group. There was no statistical difference in the mortality rate and intracranial hemorrhage transformation rate among the elderly thrombolytic group and the elderly non-thrombolytic group. These results indicated that the death risk of AIS patients could be significantly increased with the age of patients, but they did not significantly increase the hemorrhage and death risk of rt-PA thrombolysis, which were partially similar to the results of Sarikaya [21]. Indicating that rt-PA intravenous thrombolysis is safe in the elderly population aged 80 and above.

After univariate analyzing the clinical data of all elderly patients who underwent intravenous thrombolysis with rt-PA, and using their long-term prognosis as the evaluation index, we found that there were significant differences in NIHSS scores before treatment, D- dimer and heart failure history among elderly AIS patients with different long-term prognoses. D-dimer is the final product of fibrin degradation, mainly reflecting the dissolution function of fibrin, and can serve as a specific marker for thrombus formation and dissolution. Elevated D-dimer

Table 4 Comparison of clinical data in elderly AIS patients with thrombolysis with different long-term prognosis(n, mean ± SD)

Influencing factor	Good prognosis($n=16$)	Poor prognosis($n=39$)	χ^2/t	*P*
Gender				
Male(n,%)	9 (56.25)	17 (43.59)	0.730	0.393
Female(n,%)	7 (43.75)	22 (56.41)		
Age (year)	83.56 ± 2.99	84.74 ± 3.72	1.128	0.264
Weight (kg)	55.91 ± 8.84	55.27 ± 10.23	0.218	0.829
History of hypertension				
No(n,%)	3 (18.75)	6 (15.38)	0.094	0.759
Yes(n,%)	13 (81.25)	33 (84.62)		
History of hypertension				
No(n,%)	13 (81.25)	30 (76.92)	0.125	0.724
Yes(n,%)	3 (18.75)	9 (23.08)		
History of hyperlipidemia				
No(n,%)	12 (75.00)	29 (74.36)	0.002	0.960
Yes(n,%)	4 (25.00)	10 (25.64)		
History of stroke				
No(n,%)	14 (87.50)	33 (84.62)	0.076	0.783
Yes(n,%)	2 (12.50)	6 (15.38)		
History of heart failure				
No(n,%)	14 (87.50)	20 (51.28)	6.305	0.012
Yes(n,%)	2 (12.50)	19 (48.72)		
DNT (min)	64.31 ± 26.72	63.15 ± 18.72	0.183	0.855
ONT (min)	171.94 ± 45.67	159.33 ± 37.02	1.070	0.289
NIHSS score before treatment (points)	6.56 ± 3.65	16.56 ± 8.30	4.6193	0.000
Low density lipoprotein(mmol/L)	2.62 ± 0.84	2.63 ± 0.94	0. 040	0.968
High-density lipoprotein(mmol/L)	1.14 ± 0.28	1.07 ± 0.29	0.877	0.385
Homocysteine (umol/L)	14.16 ± 5.13	15.02 ± 7.57	0.412	0.682
Pre-thrombolytic systolic blood pressure(mmHg)	159.81 ± 14.30	171.56 ± 29.33	1.524	0.133
Pre-thrombolytic diastolic pressure(mmHg)	81.25 ± 11.43	88.08 ± 19.15	1.328	0.190
Random blood glucose(mmol/L)	8.10 ± 3.64	8.26 ± 4.06	0.138	0.891
Glycated hemoglobin (%)	6.21 ± 0.65	6.29 ± 1.35	0.232	0.817
White blood cell count ($\times10^9$/L)	6.53 ± 1.88	7.56 ± 2.25	1.607	0.114
Red blood cell count ($\times10^9$/L)	4.32 ± 0.54	4.16 ± 0.53	0.995	0.324
Neutrophil count ($\times10^9$/L)	3.79 ± 1.01	4.93 ± 2.27	1.922	0.060
Hemoglobin (g/L)	134.63 ± 14.10	126.72 ± 16.92	1.647	0.106
Platelet count ($\times10^9$/L)	165.25 ± 56.99	192.67 ± 60.97	1.542	0.129
PT (s)	11.19 ± 0.97	11.13 ± 0.84	0.261	0.795
APTT (s)	25.24 ± 3.24	25.55 ± 3.68	0.297	0.768
INR	0.96 ± 0.08	0.96 ± 0.08	0.119	0.905
Fibrinogen (g/L)	3.00 ± 0.50	3.23 ± 0.87	0.956	0.343
D- dimer (ug/ml)	1.09 ± 0.87	2.79 ± 2.73	2.445	0.018
Na+ (mmol/L)	140.57 ± 2.10	139.70 ± 2.60	1.191	0.239
K+ (mmol/L)	3.65 ± 0.34	3.57 ± 0.44	0.645	0.522
Urea nitrogen (mmol/L)	6.17 ± 1.38	7.09 ± 3.83	0.934	0.355
History of atrial fibrillation				
No(n,%)	8 (50.00)	15 (38.46)	0.621	0.431
Yes(n,%)	8 (50.00)	24(61.54)		
History of coronary heart disease				
No(n,%)	16 (100.00)	35 (89.74)	1.770	0.183
Yes(n,%)	0 (0.00)	4 (10.26)		
History of smoking				
No(n,%)	14 (87.50)	36 (92.31)	0.317	0.573
Yes(n,%)	2 (12.50)	3 (7.69)		

Table 5 Assignment for multivariate logistic regression analysis

Factors	Variables	Assignment
NIHSS score before treatment	X1	Continuous variable
History of heart failure	X2	No = 0, yes = 1
D- dimer	X3	Continuous variable

levels indicate the formation or degradation of blood clots in the blood vessels, which can lead to reperfusion disorders and enlargement of the infarcted area. Hsu PJ et al. found that higher levels of D-dimer were significantly associated with adverse outcomes and symptomatic cerebral hemorrhage in patients with acute ischemic stroke undergoing intravenous thrombolysis. D-dimer levels can serve as an early prognostic indicator for AIS patients receiving rt-PA treatment [22]. Heart failure in patients with acute ischemic stroke is a source of various harmful pathophysiological mechanisms, including pre thrombotic and pro-inflammatory states, deterioration of brain tissue oxygenation, and hemodynamic damage. In addition, heart failure may affect the safety and effectiveness of acute reperfusion stroke treatment. The study by Siedler G et al. showed that the presence of heart failure is an independent predictor of adverse functional outcomes in patients with acute ischemic stroke [23]. The study by Héja M et al. also suggests that heart failure is an important independent risk factor for poor outcomes in elderly patients over 80 years old with acute ischemic stroke [17].

Further binary logistic regression analysis showed that NIHSS score before treatment was an independent risk factor affecting the clinical outcome of elderly AIS patients, and that a higher NIHSS score before treatment increased the risk of poor long-term prognosis in elderly AIS patients. The reasons were analyzed as follows: The excessively high NIHSS score before treatment represented the large infarct size, great difficulty in recovering the blood supply to the penumbra, severe neurological impairment, and difficult treatment [24]. A high NHISS score represents that the more serious the nerve damage is, indicating that the recanalization rate after thrombolysis is low for patients [25].

Therefore, timely thrombolytic therapy with rt-PA considering the condition of elderly patients and paying close attention to the changes of NIHSS scores before and after treatment can effectively improve the prognosis of elderly AIS patients and reduce the risk of disability and death. Attention should also be paid to changes in D-dimer levels and a history of heart failure, which may be risk factors for poor prognosis in elderly patients with acute ischemic stroke undergoing intravenous thrombolysis. Clinical physicians still pay close attention to the blood flow of patients and timely give symptomatic treatment when the risk occurs.

This study also has limitations. Because the number of patients with acute ischemic stroke who arrived at the hospital in time during the COVID-19 pandemic decreased, the number of patients with intravenous thrombolysis decreased, and the sample size of elderly thrombolysis patients was small, so no statistical analysis was carried out on the etiology of cerebral infarction and the cause of death of elderly thrombolysis patients. There are research reports that although stroke has an impact on both men and women, gender related differences have shown specific epidemiological and clinical characteristics, and women have poorer prognosis. Women also differ from men in the distribution of risk factors, stroke subtypes, stroke severity, and outcomes [12]. The results of this study did not find any gender differences that may be related to the small sample size of elderly patients undergoing intravenous thrombolysis. Lacunar ischemic stroke is also a future research direction for this topic, because pathophysiology, prognosis and clinical features of lacunar ischemic strokes are different from all other stroke subtypes. Studies have shown that 15% of elderly stroke patients are diagnosed with lacunar infarction [11], lacunar syndrome not due to lacunar infarct accounted for 16.6% of all cases of lacunar stroke [26]. The next step is to conduct a longer study on elderly thrombolysis patients, enroll more patients, expand the sample size, reduce errors, and conduct more in-depth research on the etiology classification, causes of death, gender differences, and other factors of cerebral infarction in elderly thrombolysis patients. We will also investigate whether there are differences in the prognosis of intravenous thrombolysis between patients with lacunar and non-lacunar ischemic stroke.

Conclusion

In summary, compared with non-elderly thrombolytic patients, elderly AIS patients treated with rt-PA thrombolytic therapy have significantly reduced efficacy benefits, but still can improve the short-term and long-term prognosis. Compared with conventional elderly non-thrombolytic patients, the risks of intracranial

Table 6 Multivariate analysis of clinical outcomes in elderly patients with AIS after thrombolysis

Variable	B	SE	Wald	*P*	OR	95%CI of OR
NIHSS score before treatment	0.258	0.091	7.977	0.005	1.294	1.082 ~ 1.548
History of heart failure	-1.341	1.002	1.790	0.181	0.262	0.037 ~ 1.865
D- dimer	0.584	0.394	2.197	0.138	1.793	0.828 ~ 3.881
Constant	-1.828	1.288	2.016	0.156	0.161	-

hemorrhage conversion, and death are not significantly increased, indicating that rt-PA treatment is safe for elderly AIS patients. The NIHSS score before treatment was an independent risk factor affecting the long-term prognosis of elderly AIS patients after thrombolytic therapy. This study will help improve our understanding of the efficacy and safety of intravenous thrombolysis with alteplase in patients over 80 years old with acute ischemic stroke, make proactive decisions on ultra early intravenous thrombolysis, reduce the mortality and disability rates of stroke in the local area, and have significant social benefits.

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Author contributions
Yongyin Zhang designed and conducted the experiments, analyzed the data, and contributed to writing and editing the manuscript. Lifen Chi and Hao Shu were responsible for interpreting the data and contributed to writing and editing the manuscript. They also provided critical feedback on the study's methodology and analysis. Qiang Zhou oversaw project management and contributed to the revision of the manuscript. Qiang Zhou also provided guidance and feedback on the study's design and implementation. Shunkai Zhang provided additional oversight and contributed to the revision of the manuscript. Xuerong Huang and Xiaoyi Song provided valuable insights into the study's theoretical framework and contributed to the overall interpretation of the results. All authors played important roles in the development of the study and contributed to the final version of the manuscript.

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Data availability
The data used and/or analyzed during the current study are available from the corresponding author.

Declarations

Ethics approval and consent to participate
All patients signed an informed consent form, and this study was approved by the Medical Ethics Committee of Ruian People's Hospital (LZM2018001). We confirm that all experiments were conducted in accordance with the relevant guidelines and regulations of the Helsinki Declaration.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Mendelson SJ, Prabhakaran S. Diagnosis and Management of Transient Ischemic Attack and Acute Ischemic Stroke: A Review. JAMA. 2021 Mar 16;325(11):1088-98.
2. An JQ, Cheng YW, Guo YC, Wei M, Gong MJ, Tang YL, Yuan XY, Song WF, Mu CY, Zhang AF, Saguner AM, Li GL, Luo GG. Safety and efficacy of remote ischemic postconditioning after thrombolysis in patients with stroke. Neurology. 2020 Dec 15;95(24):e3355-e3363.
3. Mariana de Aquino Miranda J, Mendes Borges V, Bazan R, José Luvizutto G, Sabrysna Morais Shinosaki J. Early mobilization in acute stroke phase: a systematic review. Top Stroke Rehabil. 2023 Mar;30(2):157-68.
4. Schwark C, Schellinger PD. Is old age really a reason to withhold thrombolytic therapy? J Neurol Neurosurg Psychiatry. 2006;77(3):289.
5. Ohta T, Okada K, Fukuda M, Masahira N, Matsuoka T, Tsuno T, Takemura M. Safety and Efficacy of Intravenous Low-Dose Alteplase in relative contraindication patients with Acute ischemic stroke. J Stroke Cerebrovasc Dis. 2018;27(7):1844–51.
6. Longstreth WT Jr, Katz R, Tirschwell DL, Cushman M, Psaty BM. Intravenous tissue plasminogen activator and stroke in the elderly. Am J Emerg Med. 2010;28(3):359–63.
7. Sanchez S, Campos Y, Cadena A, Habib S, Deprince M, Chalouhi N, Vibbert M, Urtecho J, Athar MK, Tzeng D, Sheehan L, Bell R, Tjoumakaris S, Jabbour P, Rosenwasser R, Rincon F. Intravenous thrombolysis in the elderly is facilitated by a tele-stroke network: a cross-sectional study. Clin Neurol Neurosurg. 2020;197:106177.
8. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; American Heart Association Stroke Council. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2018 Mar;49(3):e46-e110.
9. Xu JH, He XW, Li Q, Liu JR, Zhuang MT, Huang FF, Bao GS. Higher platelet-to-lymphocyte ratio is Associated with worse outcomes after intravenous thrombolysis in Acute Ischaemic Stroke. Front Neurol. 2019;10:1192.
10. Zhang Y, Wang J, Ma Z, Mu G, Liang D, Li Y, Qian X, Zhang L, Shen F, Zhang L, Yu J, Liu Y. Prospective pilot study of tirofiban in progressive stroke after intravenous thrombolysis. Front Neurol. 2022;13:982684.
11. Arboix A, García-Eroles L, Massons J, Oliveres M, Targa C. Lacunar infarcts in patients aged 85 years and older. Acta Neurol Scand. 2000;101(1):25–9.
12. Torres-Riera S, Arboix A, Parra O, García-Erolesa L, Sánchez-López MJ. Predictive clinical factors of In-Hospital mortality in women aged 85 years or more with Acute ischemic stroke. Cerebrovasc Dis. 2024 Jan;29. https://doi.org/10.1159/000536436.
13. Psychogios K, Tsivgoulis G. Intravenous thrombolysis for acute ischemic stroke: why not? Curr Opin Neurol. 2022;35(1):10–7.
14. Thomalla G, Boutitie F, Ma H, Koga M, Ringleb P, Schwamm LH, Wu O, Bendszus M, Bladin CF, Campbell BCV, Cheng B, Churilov L, Ebinger M, Endres M, Fiebach JB, Fukuda-Doi M, Inoue M, Kleinig TJ, Latour LL, Lemmens R, Levi CR, Leys D, Miwa K, Molina CA, Muir KW, Nighoghossian N, Parsons MW, Pedraza S, Schellinger PD, Schwab S, Simonsen CZ, Song SS, Thijs V, Toni D, Hsu CY, Wahlgren N, Yamamoto H, Yassi N, Yoshimura S, Warach S, Hacke W, Toyoda K, Donnan GA, Davis SM, Gerloff C; Evaluation of unknown Onset Stroke thrombolysis trials (EOS) investigators. Intravenous alteplase for stroke with unknown time of onset guided by advanced imaging: systematic review and meta-analysis of individual patient data. Lancet. 2020 Nov 14;396(10262):1574-84.
15. Warner JJ, Harrington RA, Sacco RL, Elkind MSV. Guidelines for the early management of patients with Acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of Acute ischemic stroke. Stroke. 2019;50(12):3331–2.
16. Mowla A, Shakibajahromi B, Arora A, Seifi A, Sawyer RN, Shirani P. Thrombolysis for stroke in elderly in the late window period. Acta Neurol Scand. 2021;144(6):663–8.
17. Héja M, Fekete I, Horváth L, Márton S, Fekete KE. Experiences with intravenous thrombolysis in Acute Ischemic Stroke by Elderly Patients-A Real World scenario. Front Neurol. 2021;12:721337.
18. Bluhmki E, Danays T, Biegert G, Hacke W, Lees KR. Alteplase for Acute Ischemic Stroke in Patients Aged >80 Years: Pooled Analyses of Individual Patient Data. Stroke. 2020 Aug;51(8):2322-31.
19. Zhao XJ, Li QX, Liu TJ, Wang DL, An YC, Zhang J, Peng YB, Chen RY, Chang LS, Wang Y, Zhang L, Fan HY, Wang XJ, Zheng FX. Predictive values of CSS and NIHSS in the prognosis of patients with acute cerebral infarction: A comparative analysis. Medicine (Baltimore). 2018 Sep;97(39):e12419.
20. Duvekot MHC, Venema E, Rozeman AD, Moudrous W, Vermeij FH, Biekart M, Lingsma HF, Maasland L, Wijnhoud AD, Mulder LJMM, Alblas KCL, van Eijkelenburg RPJ, Buijck BI, Bakker J, Plaisier AS, Hensen JH, Lycklama À, Nijeholt GJ, van Doormaal PJ, van Es ACGM, van der Lugt A, Kerkhoff H,

Dippel DWJ, Roozenbeek B. PRESTO investigators. Comparison of eight prehospital stroke scales to detect intracranial large-vessel occlusion in suspected stroke (PRESTO): a prospective observational study. Lancet Neurol. 2021;20(3):213–21.
21. Sarikaya H. Safety and efficacy of thrombolysis with intravenous alteplase in older stroke patients. Drugs Aging. 2013;30(4):227–34.
22. Hsu PJ, Chen CH, Yeh SJ, Tsai LK, Tang SC, Jeng JS. High plasma D-Dimer indicates unfavorable outcome of Acute ischemic stroke patients receiving intravenous thrombolysis. Cerebrovasc Dis. 2016;42(1–2):117–21.
23. Siedler G, Sommer K, Macha K, Marsch A, Breuer L, Stoll S, Engelhorn T, Dörfler A, Arnold M, Schwab S, Kallmünzer B. Heart failure in ischemic stroke: relevance for Acute Care and Outcome. Stroke. 2019;50(11):3051–6.
24. Sun J, Lam C, Christie L, Blair C, Li X, Werdiger F, Yang Q, Bivard A, Lin L, Parsons M. Risk factors of hemorrhagic transformation in acute ischaemic stroke: a systematic review and meta-analysis. Front Neurol. 2023;14:1079205.
25. Kandregula S, Savardekar AR, Sharma P, McLarty J, Kosty J, Trosclair K, Cuellar H, Guthikonda B. Direct thrombectomy versus bridging thrombolysis with mechanical thrombectomy in middle cerebral artery stroke: a real-world analysis through National Inpatient Sample data. Neurosurg Focus. 2021;51(1):E4.
26. Arboix A, Massons J, García-Eroles L, Targa C, Comes E, Parra O. Clinical predictors of lacunar syndrome not due to lacunar infarction. BMC Neurol. 2010;10:31.

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