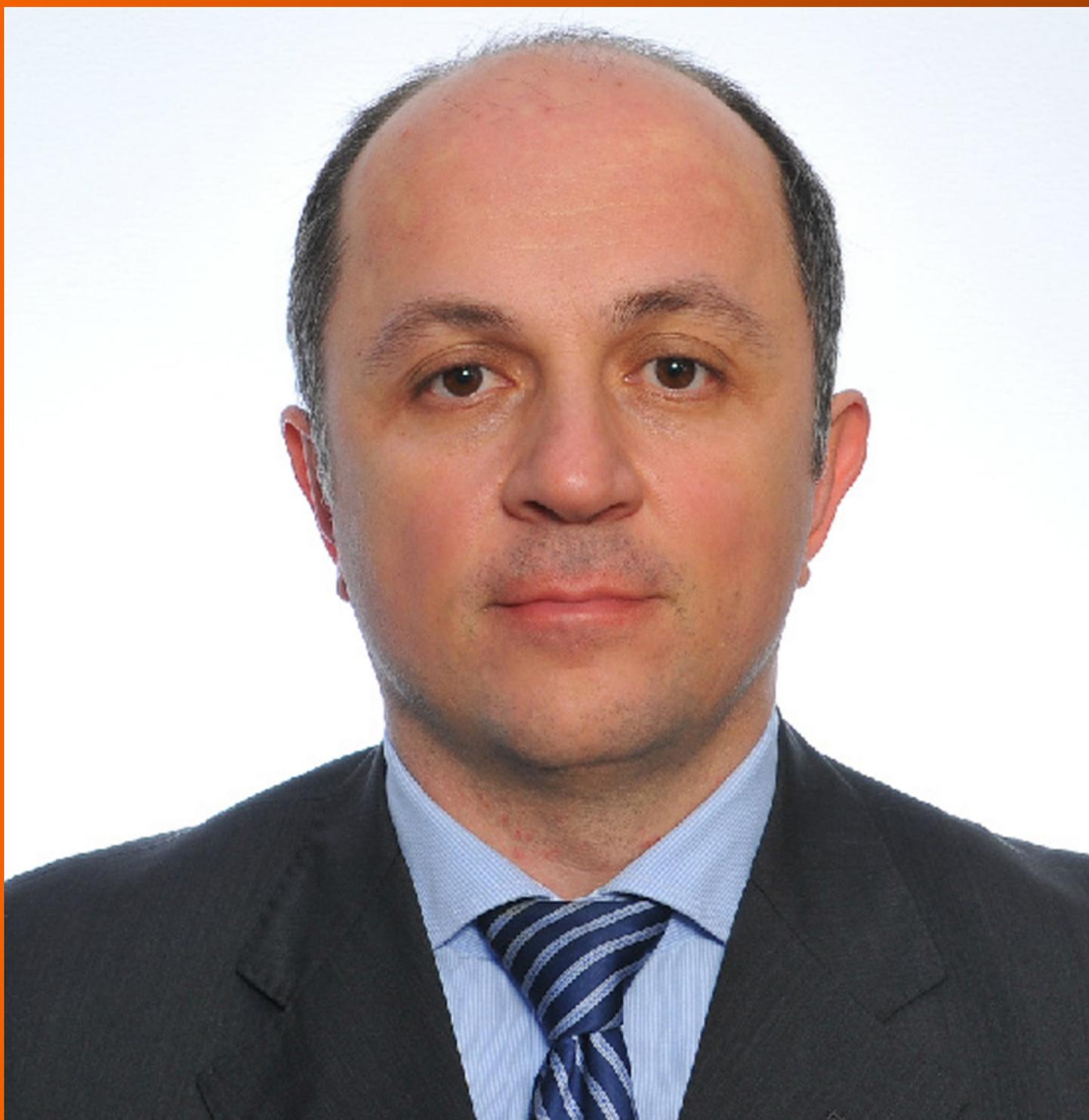


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## Observational Study

**Relationship between homocysteine level and prognosis of elderly patients with acute ischemic stroke treated by thrombolysis with recombinant tissue plasminogen activator**

Juan Li, Fan Zhou, Feng-Xue Wu

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**Author contributions:** Li J, Zhou F, and Wu FX contributed to study design and manuscript drafting; Li J, Zhou F, and Wu FX revised the manuscript; all authors proofed the manuscript for its publication.

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**Abstract****BACKGROUND**

Acute ischemic stroke (AIS) is mainly caused by cerebral blood flow disorders, which further leads to ischemic brain necrosis or encephalomalacia. The role of homocysteine (Hcy), an independent risk factor for cardiovascular disease, in the development of atherosclerosis is gradually revealed. However, studies are still rare and little is known about the relationship of Hcy level with the prognosis.

**AIM**

To explore the relationship between Hcy level and prognosis in elderly patients with AIS after thrombolytic therapy with recombinant tissue plasminogen activator (rtPA).

**METHODS**

A total of 120 patients with acute ischemic stroke who were admitted to Jingzhou Central Hospital and underwent recombinant tissue plasminogen activator treatment were randomly selected from January 2017 to December 2018. They were divided into two groups according to the level of Hcy, with 60 patients in each group. Patients with Hcy  $\geq 18.54$   $\mu\text{mol/L}$  were included into a high-level group and those with Hcy  $< 18.54$   $\mu\text{mol/L}$  were included into a low-level group. The outcomes were analyzed in the two groups after the treatment.

**RESULTS**

The National Institute of Health Stroke Scale (NIHSS) scores were significantly higher in the high-level group than in the low-level group before and 1 h after the treatment ( $P < 0.05$ ). There was no significant difference in NIHSS scores between the two groups at 12 and 24 h after the treatment ( $P > 0.05$ ). The Modified Rankin scale (MRS) scores were significantly higher in the high-level group than in the

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low-level group before and 1 h after the treatment ( $P < 0.05$ ). There was no significant difference in MRS scores between the two groups at 12 and 24 h after the treatment ( $P > 0.05$ ). NIHSS and MRS scores were positively correlated with the prognosis after thrombolytic therapy ( $P < 0.05$ ).

### CONCLUSION

The level of Hcy is closely related to the prognosis of elderly patients with acute ischemic stroke, and after rtPA treatment, the prognosis of elderly patients is improved significantly.

**Key words:** Hcy level; Acute ischemic stroke; Thrombolytic therapy; Prognosis

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**Core tip:** Acute ischemic stroke (AIS) is one of the most common strokes that occur in the clinical practice. It is mainly caused by cerebral blood flow disorders, which further leads to ischemic brain necrosis or encephalomalacia. Studies are still rare and little is known about the relationship of Hcy level with the prognosis. The present study analyzed the relationship between homocysteine level and the prognosis of elderly patients with AIS after the administration of recombinant tissue plasminogen activator.

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## INTRODUCTION

Acute ischemic stroke (AIS) is one of the most common strokes that occur in the clinical practice. It is mainly caused by cerebral blood flow disorders, which further leads to ischemic brain necrosis or encephalomalacia<sup>[1,2]</sup>. For these patients, early therapeutic strategy, especially the widely used revascularization and intravesical therapy, should be used to reduce disability and death rates. A study by Li *et al*<sup>[3]</sup> shows that intravenous thrombolysis is the most commonly used reperfusion therapy for stroke, and early application of the thrombolytic agent, recombinant tissue plasminogen activator (rtPA), is safe and effective in patients within 4.5 h after the onset of AIS. Meanwhile, the role of homocysteine (Hcy), an independent risk factor for cardiovascular disease, in the development of atherosclerosis is gradually revealed. However, studies are still rare and little is known about the relationship of Hcy level with the prognosis<sup>[4]</sup>. The present study analyzed the relationship between Hcy level and the prognosis of elderly patients with AIS after the administration of rtPA.

## MATERIALS AND METHODS

### Participants

A total of 120 patients with AIS admitted to Jingzhou Central Hospital from January 2017 to December 2018 were randomly selected. They were assigned to either a high-level group or a low-level group according to the level of Hcy, with 60 patients in each group. The eligibility criteria for the study included: patients who did not have a history of intracranial hemorrhage and patients who provided informed consent along with their family members; patients in whom measures were taken within 4.5 h after the onset of AIS; patients in whom computed tomography/magnetic resonance imaging scanning indicated anterior circulation syndrome before thrombolysis. However, patients with severe brain injury or previous stroke, patients who had a history of myocardial infarction, patients with mental disorders and speech and language impairments, and patients who were unwilling to participate in the study were excluded from the study. The high-level group included 60 patients aged 81 to 89 years, with 35 male patients, 25 female patients, and an average age of  $84.6 \pm 1.7$

years. The low-level group included 60 patients aged 80 to 88 years, with 36 male patients, 24 female patients, and an average age of (85.6 ± 1.8) years. There was no significant difference in the general characteristics of the patients between the two groups ( $P > 0.05$ ).

### Methods

Patients were intravenously given rtPA 0.9 mg/kg produced by Shandong Ehua Biological Pharmaceuticals Co., Ltd (National Drug Code: S20070023, 18 mg/mL) with the first 10% IV bolus administered and the rest continuously infused for 1 h. Clinicians were required to closely monitor the changes in patients' conditions during the medication administration and at 24 h after the treatment. Patient's blood pressure was measured and recorded every 15 min. Neurological function was assessed every 30 min for 6 h followed by the assessment every 60 min up to 24 h after the treatment.

### Measurements

The NIH Stroke Scale (NIHSS)<sup>[5]</sup> was used to score the neurological function. Patients with higher NIHSS scores also had higher degree of neurologic deficit. If the NIHSS score decreased by 4 at 7 d after the intravenous thrombolysis, it indicated that the early treatment is effective. The modified Rankin scale (MRS)<sup>[6]</sup> was used to evaluate the function disorders and disability in patients at 14 d after the onset of the stroke. An MRS score ≤ 2 indicated that patients can take care of themselves and an MRS score ≥ 3 indicated that patients cannot take care of themselves. The relationship was analyzed between Hcy level and the prognosis of patients with AIS after the administration of rtPA.

### Statistical analysis

SPSS19.0 was used for the calculating scores and values in the study. The results were compared by the chi-square test or *t*-test. "The count data are presented as percentages and the measured data are presented as the mean ± standard deviation. *P*-values less than 0.05 were considered statistically significant.

---

## RESULTS

### *NIHSS scores in the two groups before and after the treatment*

NIHSS scores were significantly higher in the high-level group than in the low-level group before the treatment and at 1 h after the treatment ( $P < 0.05$ ). However, there was no significant difference in the NIHSS scores between the two groups at 12 and 24 h after the treatment ( $P > 0.05$ , Table 1).

### *MRS scores in the two groups before and after the treatment*

Before the treatment and at 1 h after the treatment, MRS scores were significantly higher in the high-level group than in the low-level group ( $P < 0.05$ ). However, there was no significant difference in the MRS scores between the two groups at 12 and 24 h after the treatment ( $P > 0.05$ , Table 2).

### *Relationship between Hcy level and prognosis after thrombolysis*

NIHSS and MRS scores were positively associated with the prognosis of elderly patients with AIS who underwent thrombolysis with rtPA ( $P < 0.05$ , Table 3).

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## DISCUSSION

Elderly population has a high risk for cerebrovascular disease and AIS. According to previous data, about 50% of patients with AIS are more than 85 years. If treatment measures are performed on these patients, it is nearly impossible for more than 30% of patients to obtain the most effective treatment when age was considered as an indication for thrombolytic therapy<sup>[7]</sup>. However, the results of the Third International Stroke Trial support thrombolytic therapy for elderly patients. The benefits of thrombolytic therapy are far greater than those of non-thrombolytic therapy, although the risk for hemorrhage and incidence of mortality were comparatively high and the prognosis was comparatively poor in patients who received thrombolysis<sup>[8]</sup>. The above studies revealed that thrombolytic therapy can be taken irrespective of age in patients with AIS. Currently, the most commonly used effective agent for thrombolysis is rtPA<sup>[9]</sup>. According to the Chinese expert consensus, for patients with AIS, if the continuous parameters are controlled within 3 h, clinicians should identify the benefits of thrombolysis in patients within 3 to 4.5 h and tailor medical treatment

**Table 1 Comparison of National institute of Health Stroke Scale scores between the two groups before and after the treatment (n = 60)**

Groups	Before treatment	1 h after treatment	12 h after treatment	24 h after treatment
High-level group	13.25 ± 3.56	10.26 ± 2.56	6.89 ± 1.96	5.12 ± 1.56
Low-level group	9.56 ± 2.65	7.56 ± 1.56	6.22 ± 2.02	4.84 ± 1.26
<i>t</i>	6.440	6.976	1.844	1.082
<i>P</i>	0.000	0.000	0.068	0.282

to the individual characteristics of each patient to effectively reduce the incidence of adverse reactions and to benefit more patients with AIS in clinical practice.

Harris *et al*<sup>[11]</sup> confirmed that Hcy level was an important factor to predict the prognosis of patients with AIS. A high Hcy level indicated a high severity of neuropathy and increased volume of hemorrhage. That is because high Hcy level will lead to damage to the vascular wall and blood-brain barrier and even damage to the cerebral artery and matrix of endothelial cells. Moreover, increased free radicals from hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) will exacerbate endothelial dysfunction<sup>[12]</sup>. Hcy level is an important factor in predicting the prognosis of thrombolysis, which is associated with limited report on the assessment of risks in elderly patients receiving thrombolysis<sup>[13]</sup>. The results of the present study revealed that NIHSS scores were improved and high Hcy level gradually went back to normal, which was not significantly different from low Hcy level ( $P > 0.05$ ). It further demonstrated that high Hcy level could cause short-term neurological deterioration and a poor prognosis. Therefore, Hcy is one of the most important items to test the prognosis of patients with AIS receiving thrombolysis.

As showed in Table 2, by analyzing the MRS scores, it was revealed that cerebral nerves partially recovered after the treatment in the high-level group compared with the low-level group ( $P < 0.05$ ). Genoud *et al*<sup>[14]</sup> established that rtPA as a plasminogen activator can dissolve the blood clot in a short term, enhance the recovery of local blood flow, and reduce cerebral tissue injury. Hcy is a common type of testing item. Patient's condition is improved after the treatment and the Hcy level decreased accordingly. For patients with AIS receiving thrombolysis, NIHSS and MRS scores are associated with the prognosis of thrombolysis ( $P < 0.05$ ). An epidemiological study<sup>[15]</sup> showed that Hcy is a vulnerable and changeable risk factor which is influenced by several factors. Per reduction of 3  $\mu\text{mol/L}$  of Hcy level is associated with a decrease of 10% in the risk of stroke. According to the above study, Hcy is an important factor to predict the prognosis of elderly patients with AIS receiving thrombolysis.

In conclusion, Hcy level is associated with the prognosis of elderly patients with AIS. After the treatment with rtPA, the prognosis of patients is significantly improved.

**Table 2 Comparison of Modified Rankin scale scores between the two groups before and after the treatment (n = 60)**

Groups	Before treatment	1 h after treatment	12 h after treatment	24 h after treatment
High-level group	3.25 ± 1.05	2.95 ± 0.89	2.15 ± 0.58	2.06 ± 0.48
Low-level group	2.15 ± 0.59	2.06 ± 0.45	1.99 ± 0.44	1.92 ± 0.42
<i>t</i>	5.746	6.913	1.702	1.700
<i>P</i>	0.000	0.000	0.091	0.092

**Table 3 Relationship between homocysteine levels and prognosis after thrombolysis**

	Hcy levels	
	<i>r</i>	<i>P</i>
NIHSS scores	0.486	< 0.05
MRS scores	0.567	< 0.05

Hcy: Homocysteine; NIHSS: National Institute of Health Stroke Scale; MRS: Modified Rankin scale.

## ARTICLE HIGHLIGHTS

### Research background

Acute ischemic stroke (AIS) is mainly caused by cerebral blood flow disorders, which further leads to ischemic brain necrosis or encephalomalacia. The role of homocysteine (Hcy) for cardiovascular disease in the development of atherosclerosis is gradually revealed.

### Research motivation

Studies are rare and little is known about the prognostic role of Hcy in AIS.

### Research objectives

To explore the relationship between Hcy level and prognosis in elderly patients with AIS after thrombolytic therapy with recombinant tissue plasminogen activator (rtPA).

### Research methods

A total of 120 patients with AIS who underwent rtPA therapy were randomly selected. They were divided into two groups according to the level of Hcy, with 60 patients in each group. Patients with Hcy ≥ 18.54 μmol/L were included into a high-level group and those with Hcy < 18.54 μmol/L were included into a low-level group. The outcomes of the patients were analyzed after the treatment.

### Research results

The National Institute of Health Stroke Scale (NIHSS) scores were significantly higher in the high-level group than in the low-level group before and 1 h after the treatment. The Modified Rankin scale (MRS) scores were also significantly higher in the high-level group than in the low-level group before and 1 h after the treatment. NIHSS and MRS scores were positively correlated with the prognosis after thrombolytic therapy.

### Research conclusions

Hcy level is associated with the prognosis of elderly patients with AIS. After treatment with rtPA, the prognosis of patients is significantly improved.

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