Submitted: 17 October, 2023 Accepted: 23 January, 2024 Published: 08 March, 2024 DOI:10.22514/sv.2024.031

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ORIGINAL RESEARCH

Effect of multidisciplinary refined time management combined with organized stroke management on the efficacy of intravenous thrombolysis in patients with acute ischemic stroke

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Abstract

This study aims to investigate the effects of multidisciplinary refined time management combined with organized stroke management in intravenous thrombolysis on patients with acute ischemic stroke. 226 acute ischemic stroke patients treated with intravenous thrombolysiswere selected for retrospective analysis. A Control group participants underwent organized stroke management, whereas study group participants underwent multidisciplinary refined time management based on the control group. The study group responded to intravenous thrombolysis for 24 hours at an overall rate of 92.92%, significantly higher than 79.65% in the control group ($p < 0.05$). The time from onset to emergency, time for National Institute of Health Stroke Scale (NIHSS) scoring by emergency doctors, consultation time for neurologists, judgement time for head computed tomography (CT), interpretation time for examination results, communication time with family members to sign the consent form, and time from admission to medication in the study group were significantly shorter than that in control group ($p < 0.05$). The incidence of hemorrhagic transformation, six-month mortality and six-month rehospitalization rate in the study group were significantly lower than those in the control group ($p < 0.05$). Before thrombolysis, cerebrovascular reserve function and neurological function indexes in both groups were improved, and there was significant difference before and after thrombolysis in this group ($p > 0.05$); After thrombolysis, mean blood flow velocity (MFV) and breath-holding index (BHI) in the study group were significantly higher than those in the control group ($p < 0.05$); pulsatility index (PI) was lower than that in the control group, showing a significant difference ($p < 0.05$); Serum nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) were significantly higher than those in the control group ($p < 0.05$). Multidisciplinary refined time management combined with organized stroke management can improve the effect of intravenous thrombolysis in acute ischemic stroke.

Keywords

Multidisciplinary refinement; Time management; Organized stroke management; Acute ischemic stroke; Intravenous thrombolysis

1. Introduction

Stroke emerges as a common cerebrovascular disease, resulting from brain tissue injury or necrosis triggered by cerebrovascular obstruction or rupture. A number of factors, including age, lifestyle, primary diseases and drug diet, can contribute to the disease. It is more prevalent in smokers, alcoholics and patients taking long-term platelet inhibitors or anticoagulant medications. Ischemic stroke is the main type of stroke, usually onset after sleep or morning rise. It shows dizziness, headache, limb numbness, nausea, vomiting and dysphagia. Besides, patients may experience dyskinesia and slurred speech. Without timely intervention, patients can suffer from brain hernias and other complications and even face life-threatening consequences [1]. Intravenous thrombolysis is the major treatment for ischemic stroke. Intravenous infusion allows thrombolytic drugs to be infused into the body through the peripheral vein or central vein to prevent thrombosis, facilitate blood circulation at the lesion site, and promote thrombolysis [2]. However, a strict time window applies to intravenous thrombolysis. Patients generally wait a long time before receiving thrombolysis, miss the optimal treatment time, and only a few are treated within 3 hours of onset [3]. To improve clinical treatment effects and shorten patients' waiting time before thrombolysis, optimizing and improving stroke management is of great clinical importance. Shortening the time from admission to medication for stroke patients to ensure the thrombolytic effect can save the patient's life and improve the patient's prognosis. Organized stroke management in clinical practice has gained popularity in recent years [4]. A multidisciplinary collaboration is required, as well as integration of medical plans. On this basis, to further strengthen stroke management, our hospital introduced multidisciplinary refined time management into clinical practice, scientifically dividing treatment time according to the fact that ischemic stroke requires urgent treatment. We implemented more refined targeted management, achieving improved clinical outcomes [5]. Therefore, to investigate the role of multidisciplinary refined time management combined with organized stroke management in intravenous thrombolysis for acute ischemic stroke patients, relevant patients admitted to our hospital were selected for this study.

2. Materials and methods

2.1 General information

A total of 226 patients with acute ischemic stroke treated with intravenous thrombolysis in our hospital from January 2020 to January 2023 were enrolled and divided into study group and control groups according to management methods. The study group consisted of 113 patients. There were 60 males and 53 females, aged 48–85 years (mean: 65.72 ± 5.12 years). Imaging characteristics: 27 cases of lacunar infarction (maximum lesion $<$1.5 cm), 65 cases of small infarction (1.5 cm $\leq$ maximum lesion $\leq$ 3.0 cm), 21 cases of large infarction (more than 1 lesion $>$5.0 cm), and body mass index: 18.5–25.0 kg/m^2 (mean: 21.78 ± 1.12 kg/m^2). The control group consisted of 113 patients. There were 65 males and 48 females, aged 50–82 years (mean: 65.21 ± 5.44 years). Imaging characteristics: 30 cases of lacunar infarction, 68 cases of small infarction, 15 cases of large infarction, and body mass index: 18.8–24.5 kg/m^2 (mean: 21.56 ± 1.36 kg/m^2).

Inclusion criteria: (1) patients with acute ischemic stroke; (2) meet the indications for intravenous thrombolysis; (3) time from onset to admission is less than 4.5 h; (4) complete medical records that support for the study.

Exclusion criteria: (1) patients with severe heart, liver, kidney and other tissue and organ lesions; (2) patients with other similar diseases (cerebral hemorrhage, cerebral embolism, intracranial space-occupying injury, chronic subdural hematoma); (3) patients who received other treatment; (4) patients with a history of brain tissue trauma or surgery within 6 months; (5) patients with mental illnesses (schizophrenia, bipolar disorder, mania, depression, personality disorder).

Comparability showed no significant difference between the two groups ($p > 0.05$).

2.2 Methods

Patients in control group received organized stroke management, developed a multidisciplinary treatment plan, and were provided with enhanced stroke management based on the following process:

(1) Neurosurgery assessed patients' condition, intravenous thrombolytic therapy was performed by experienced attending physicians, and urokinase and alteplase were selected in accordance with patients' condition;

(2) Neurology department evaluated patients' condition after intravenous thrombolytic therapy and provided Electrocardiogram (ECG) monitoring, cerebral protection and other non-surgical treatments;

(3) A rehabilitation plan is developed based on the post-operative recovery of the patients, which was supervised and guided throughout training by a specially-assigned person;

(4) Knowledge education members educate patients and their families about the disease and intravenous thrombolysis and provide life guidance for the patients.

Patients in study group received multidisciplinary refined time management on the basis of the control group:

(1) Formulate time node management plans:

According to the patient treatment process, the treatment time was divided into the following 7 nodes: the time from onset to arrival in the emergency department, time for NIHSS scoring by emergency doctors, consultation time for neurologists, interpretation time for head CT results, interpretation time for examination results, communication time with the family members to sign the consent form, as well as the Door to Needle Time (DNT).

(2) Strengthen time node management:

Stroke management was strengthened according to 7 time nodes, which required the personnel responsible for different nodes to complete their respective tasks within the specified time, and further shortened the node's duration to ensure the efficacy of intravenous thrombolysis.

(3) Establish green channel for stroke:

A time management form was developed for intravenous thrombolysis in stroke patients. Time points when all patients entered the green channel were recorded by a specially-assigned person. Monthly summaries were provided. A problem analysis was conducted, and improvement measures were suggested to improve management quality.

(4) Strengthen supervision and control:

Data were recorded and tracked in the hospital according to the nodes. Meanwhile, supervision and control were performed.

(5) Strengthen training and assessment:

The hospital periodically organizes staff in stroke management to perform professional training. It implements assessment and links assessment with performance pay.

2.3 Outcome measures

2.3.1 Efficacy of intravenous thrombolysis for 24 hours in both groups

According to the National Institute of Health Stroke Scale (NIHSS), determine thrombolysis efficacy for 24 hours by comparing the difference between before thrombolysis and 24 hours after thrombolysis. If the difference value is not less than 6 points, it is a marked response; if the difference value is less than 3 points, it is a moderate response; if 3 points $<$ difference value $<$ 6 points, it is no response; if the overall response rate = (marked response cases + moderate response cases)/total cases $\times$ 100%.

2.3.2 Time for each link of thrombolysis process in both groups

The time from onset to emergency, NIHSS scoring time of emergency doctors, consultation time for neurologists, determination time for head CT results, interpretation time of test results, communication time with family members and time from admission to medication were compared between the control group and study groups.

2.3.3 Clinical outcomes in both groups

Both groups were followed up for 6 months after intravenous thrombolysis. The control and study groups were compared for hemorrhagic transformation (oozing of infarcted brain tissue 24 hours after thrombolysis), six-month mortality, and six-month rehospitalization rates.

2.3.4 Cerebrovascular reserve function indicators in both groups

Before thrombolysis and 24 h after thrombolysis, an ultrasound transcranial Doppler blood flow analyzer (manufacturer: Jiangsu Yikang Electronic Technology Co., Ltd., registration certificate No. 20182070620: model specification: EK-1000A, Xuzhou, China) was used to detect mean blood flow velocity (MFV), pulsatility index (PI) and breath-holding index (BHI).

2.3.5 Neurological function indexes in both groups

Venous blood was drawn from patients before thrombolysis and 24 hours after thrombolysis. Venous blood samples (3–5 mL) were collected from patients before thrombolysis and 24 h after thrombolysis, respectively, then centrifuged for treatment in a medical centrifuge (manufacturer: Zhejiang Borumon Biological Technology Co., Ltd. filing number: 20160031, model specification: type III, Hangzhou, China). Speed: 3500 r/min, radius: 12 cm, duration: 5 min. Serum nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) levels were measured using an automatic biochemical analyzer (manufacturer: Dirui Medical Technology Co., Ltd., registration certificate number: 20192220224, model specification: CS-1200, Changchun, China). The detection method was an enzyme-linked immunosorbent assay (ELISA).

2.4 Statistical methods

Data were analyzed by IBM SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA). Enumeration data indicated percentages (%) and χ^2 for the test. Continuous data are presented as mean ($\bar{x}$) $\pm$ standard deviation (s). Measurement data are in normal distribution; $\bar{x} \pm s$and t indicate tests. $p < 0.05$ demonstrated a significant difference.

3. Results

3.1 Efficacy of intravenous thrombolysis for 24 hours in both groups

The study group responded to intravenous thrombolysis for 24 hours at an overall rate of 92.92%, significantly higher than 79.65% in the control group ($p < 0.05$), as shown in Table 1 and Fig. 1.

3.2 Time of each link of thrombolysis process in both groups

The time from onset to emergency treatment, time for NIHSS scoring by emergency doctors, consultation time for neurologists, judgment time for head CT results, interpretation time for examination results, communication time with family members to sign the consent form and time from admission to medication in the study group were significantly shorter than that in the control group ($p < 0.05$), as presented in Table 2 and Fig. 2.

3.3 Clinical outcomes in both groups

The incidence of hemorrhagic transformation, six-month mortality and six-month rehospitalization rate in the study group were significantly lower than those in the control group ($p < 0.05$), as revealed in Table 3.

3.4 Cerebrovascular reserve function indexes in both groups

Before thrombolysis, there were no significant differences in cerebrovascular reserve function indexes between the two groups ($p > 0.05$). After thrombolysis, cerebrovascular reserve function indexes significantly improved in both groups, with significant difference before and after thrombolysis ($p < 0.05$). MFV and BHI after thrombolysis in the study group were significantly higher than those in the control group ($p < 0.05$). PI after thrombolysis was lower than that in the control group, showing a significant difference ($p < 0.05$), as shown in Table 4.

3.5 Comparison of neurological function between both groups

Before thrombolysis, there were no significant differences in neurological function indexes between both groups ($p > 0.05$). After thrombolysis, the neurological function indexes of the two groups were significantly improved ($p < 0.05$). NGF, BDNF and NT-3 after thrombolysis in the study group were significantly higher than those in the control group ($p < 0.05$), as shown in Table 5.

4. Discussion

Acute ischemic stroke is a devastating disease associated with high mortality and disability rates, threatening patients' lives [6]. To dissolve thrombus and improve blood supply to brain tissue, venous embolism is often used. However, intravenous

TABLE 1. Efficacy of intravenous thrombolysis for 24 hours in both groups (n (%)).

Group	Case	Marked response	Moderate response	No response	Overall response rate
Study group	113	65 (57.52)	40 (35.40)	8 (7.08)	105 (92.92)
Control group	113	55 (48.67)	35 (30.97)	23 (20.35)	90 (79.65)
χ^2 value					8.412
p value					0.004

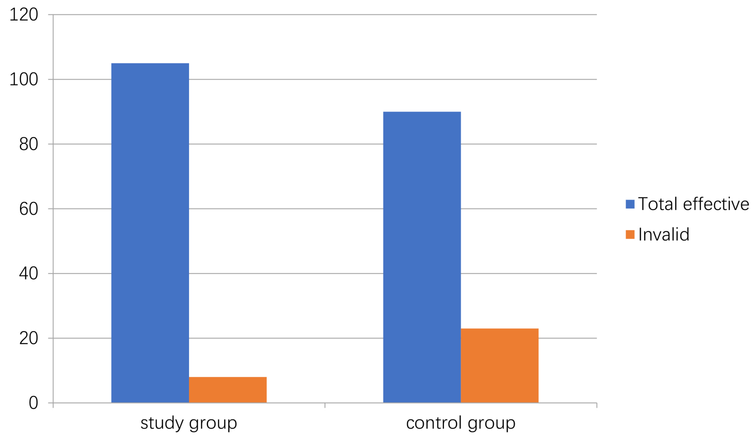

FIGURE 1. Efficacy plot of intravenous thrombolysis for 24 h in the two groups.

TABLE 2. Time of each link of thrombolysis process in both groups ($\bar{x} \pm s$, min).

Indicator	Study group (n = 113)	Control group (n = 113)	t value	p value
Time from onset to emergency treatment	128.16 ± 10.32	182.21 ± 16.78	29.166	<0.001
Time for NIHSS scoring by emergency doctors	2.72 ± 0.54	5.56 ± 0.52	53.833	<0.001
Consultation time for neurologists	5.36 ± 0.50	8.96 ± 0.72	45.910	<0.001
Judgment time for head CT results	22.24 ± 1.96	35.80 ± 3.16	38.764	<0.001
Interpretation time for examination results	33.68 ± 2.78	50.12 ± 4.48	33.146	<0.001
Communication time with family members to sign the consent form	12.72 ± 0.96	17.54 ± 1.21	33.173	<0.001
Time from admission to medication	48.12 ± 4.21	72.96 ± 6.54	33.949	<0.001

NIHSS: National Institute of Health Stroke Scale; CT: computed tomography.

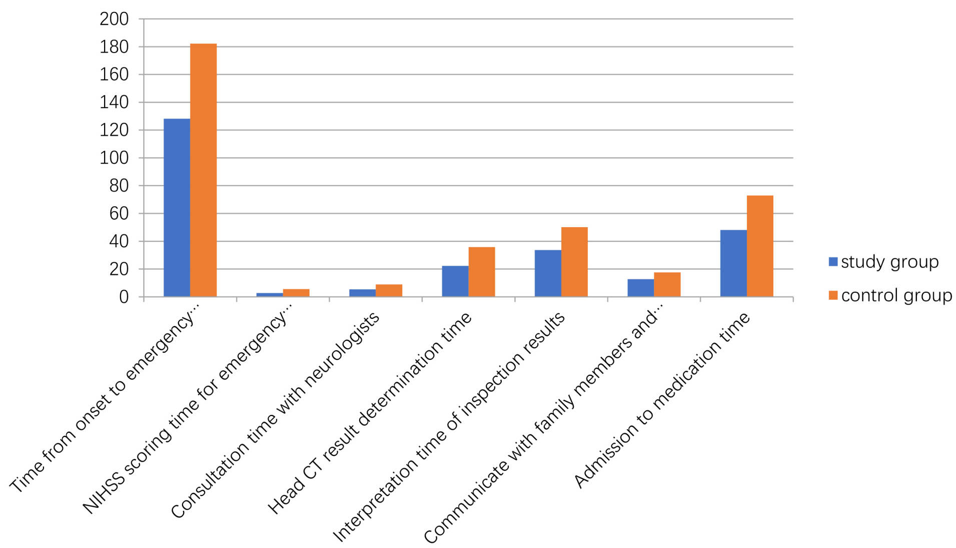

FIGURE 2. Time map of each link of thrombolysis process in the two groups. NIHSS: National Institute of Health Stroke Scale; CT: computed tomography.

TABLE 3. Clinical outcomes in both groups (n (%)).

Group	Case	Hemorrhagic transformation	Six-month mortality	Six-month rehospitalization
Study group	113	3 (2.65)	0 (0.00)	2 (1.77)
Control group	113	12 (10.62)	7 (6.19)	10 (8.85)
χ^2 value		5.784	5.307	5.632
p value		0.016	0.021	0.018

TABLE 4. Cerebrovascular reserve function indexes in both groups ($\bar{x} \pm s$).

Indicator	Study group (n = 113)	Control group (n = 113)	t value	p value
Before thrombolysis	62.78 ± 5.12	63.16 ± 5.44	0.541	0.589
After thrombolysis	76.18 ± 6.45	68.21 ± 5.72	9.827	<0.001
MFV (cm/s)				
t value	17.297	6.801		
p value	<0.001	<0.001		
Before thrombolysis	0.81 ± 0.07	0.82 ± 0.06	1.153	0.250
After thrombolysis	0.66 ± 0.05	0.74 ± 0.07	9.886	<0.001
PI (U/mL)				
t value	18.536	9.224		
p value	<0.001	<0.001		
Before thrombolysis	0.62 ± 0.05	0.61 ± 0.05	1.503	0.134
After thrombolysis	0.83 ± 0.07	0.72 ± 0.06	12.683	<0.001
BHI (ng/mL)				
t value	25.95	14.972		
p value	<0.001	<0.001		

MFV: blood flow velocity; PI: pulsatility index; BHI: breath-holding index.

TABLE 5. Comparison of neurological function between both groups ($\bar{x} \pm s$, ng/mL).

Indicator	Study group (n = 113)	Control group (n = 113)	t value	p value
Before thrombolysis	115.12 ± 10.24	114.72 ± 10.18	0.294	0.759
After thrombolysis	132.16 ± 10.78	122.32 ± 11.21	6.726	<0.001
NGF				
t value	12.183	5.335		
p value	<0.001	<0.001		
Before thrombolysis	10.72 ± 0.78	10.78 ± 0.75	0.589	0.556
After thrombolysis	16.54 ± 1.52	13.12 ± 1.27	18.354	<0.001
BDNF				
t value	36.213	16.865		
p value	<0.001	<0.001		
Before thrombolysis	7.12 ± 0.56	7.18 ± 0.54	0.820	0.413
After thrombolysis	12.54 ± 1.18	9.80 ± 0.81	20.350	<0.001
NT-3				
t value	44.111	28.609		
p value	<0.001	<0.001		

NGF: nerve growth factor; BDNF: brain-derived neurotrophic factor; NT-3: neurotrophin-3.

thrombolysis has a time window of approximately 4.5 hours following onset. Beyond this time period, it shows brain cell necrosis and degeneration. Even with thrombolytic therapy, blood perfusion is difficult to restore, affecting brain tissue regeneration [7]. Therefore, intravenous thrombolysis management is necessary to pay attention to patients with acute ischemic stroke to provide early treatment, ensure the thrombolytic effect, and improve the prognosis.

Stroke patients are commonly managed through organized stroke management. It is possible to improve the therapeutic effect of stroke by establishing relevant departments as stroke units and providing them with all-round and holistic care [8]. Through multidisciplinary refined time management, the intravenous thrombolysis process is divided according to time and independent at different time points. This can save treatment time while improving medical staff enthusiasm [9]. In combination with clinical experience, we successfully integrated both into managing acute ischemic stroke, achieving positive clinical results.

NIHSS is an important index to evaluate the therapeutic effect of acute ischemic stroke, along with intravenous thrombolysis regimens for anterior and posterior circulation strokes. In general, posterior circulation has a poor prognosis and a high NIHSS score. In the study group, intravenous thrombolysis for 24 hours resulted in a higher overall response rate than in the control group, which showed that the combined management method could significantly improve the therapeutic effect. According to the analysis, the shortened redundant time between different departments could be achieved through combined multidisciplinary refined time management based on organized stroke management. Due to close cooperation between departments, work efficiency was significantly improved. The time from admission to diagnosis and treatment of patients was evidently shortened, and intravenous thrombolysis effects were improved [10].

Multidisciplinary refined time management builds a green channel for intravenous thrombolysis in patients with acute ischemic stroke, allowing for the division of labor and cooperation of different disciplines, encompassing the characteristics of refined, organized and multidisciplinary treatment cooperation. It reduces unnecessary time consumption, strives for intravenous thrombolysis time for patients beyond the thrombolysis time window, and increases thrombolysis proportion [11]. The study group took shorter to complete each link than the control group, which indicated that optimizing intravenous thrombolysis management processes for acute ischemic stroke could prompt patients to seek medical attention as soon as possible, reduce treatment time and improve prognosis. Most patients with acute ischemic stroke are ineligible for intravenous thrombolysis because of time delays, primarily from admission to medication. Multidisciplinary refined time management may improve the medical staff enthusiasm, and significantly shorten the time and connection time spent on each link in intravenous thrombolysis. Moreover, it can significantly reduce the controllable time consumption of medical care, enable a tightly integrated treatment process and shorten the treatment time.

Hemorrhage converts to intracranial hemorrhagic lesions, which are also common after intravenous thrombolysis and are compromised by recanalization of occluded vessels and reperfusion injury [12]. Factors such as intravenous thrombolytic drugs influence incidence and development, which affects prognosis. In this study, there were no deaths in the observation group and 7 deaths in the control group. 4 patients died from increased infarct during follow-up, 2 from brain herniation, and 1 from recurrent subarachnoid hemorrhage. A lower rate of hemorrhagic transformation, six-month mortality and six-month rehospitalization were observed in the study group, showing that a combination of multidisciplinary refined time management and organized stroke management can strive for the best time for patients to receive intravenous thrombolytic therapy, maximizing its effect. Furthermore, it can reduce adverse events such as hemorrhagic transformation, improve stroke symptoms, and reduce readmission and death risk.

Despite pathological stimulation, cerebral blood flow remains normal in acute ischemic stroke patients, and arterioles and capillaries are mostly regulated by contractions or dilatations to maintain brain function, a condition known as cerebrovascular reserve that can influence the prognosis [13]. MFV can be used to assess the degree of vascular stenosis. A degree of diameter stenosis of less than 50% doesn't necessarily result in hemodynamic changes [14]. In acute ischemic stroke patients, cerebral blood flow velocity and blood flow are reduced, and blood supply is interrupted, causing cerebral ischemia and hypoxia, leading to symptoms. PI is an important parameter that describes spectral characteristics. It is calculated from blood flow velocity and affected by the difference between systolic and diastolic blood flow values. A greater difference value indicates a greater PI value, which measures reverse intravascular perfusion or distal vascular resistance. When cerebral vessels are normal, intracranial vessels have relatively low pulsatile waveforms and peripheral vessels have relatively high pulsatile waveforms. After an acute ischemic stroke, intracranial arterial pressure increases, resulting in an increase in PI. In stroke patients, a breath holding test can assess cerebrovascular reactivity. CO_2 regulates cerebrovascular blood flow and relaxes vascular smooth muscle. By increasing CO_2 partial pressure, it reduces brain tissue pH after penetrating the blood-brain barrier, promotes vascular smooth muscle relaxation, increases blood flow and velocity, and conversely decreases blood flow and velocity. Brain reactivity was assessed by BHI, which is easy to perform without medication, safe and feasible [15]. The study group had higher MFV and BHI, while PI was lower. With organized stroke management and multidisciplinary refined time management in intravenous thrombolytic therapy for patients with acute ischemic stroke, it can be realized through division of labor and cooperation between various departments. Also, it can enhance the positive initiative of medical staff in all aspects of thrombolytic therapy, reduce time delays, maximize the thrombolytic effect, and improve cerebral blood flow status and reserve function.

Patients with acute ischemic stroke can suffer neurological damage and develop a series of sequelae, so neurological parameters can be detected to assess the management effect. NGF is a trophic factor secreted by the central nervous system that promotes nerve growth and development. After an acute ischemic stroke, nerve growth is inhibited, negatively affecting the neurological function of patients [16]. In the central nervous system, the most abundant neurotrophic factor, BDNF, plays a variety of biological roles, such as preventing neuronal death from injury, promoting regeneration and differentiation of injured neurons, and improving neurons' pathological status. Patients consume a large amount of BDNF after onset, resulting in a rapid decrease in its level [17]. NT-3 was discovered after real-time fluorescence quantification and gene library screening of NGF and BDNF homologous sequences with strong homology. It is evenly expressed across a variety of tissues and promotes biological growth, development, and neural tissue repair [18]. These indicators can not only be used to determine whether a patient is sick but also to assess the severity of the disease. Generally, the more severe the stroke, the more significant the inhibition of neurological function. It can cause neurotrophin levels to drop far below normal. In this study, various neurological function indicators were higher in the study group, suggesting that in the management of organized stroke with intravenous thrombolysis in acute ischemic stroke, the use of multidisciplinary refined time management can be effective in intravenous thrombolysis, promoting thrombolysis, relieving neurological deficit symptoms, and improving neurological function.

5. Conclusions

A multidisciplinary refined time management strategy in conjunction with organized stroke management results in improved intravenous thrombolysis effects in acute ischemic stroke, shorter presentation times, improved vascular reserve function and neurological function, as well as improved clinical outcomes, which can be promoted.

In addition to the limitations of the number and source of cases, this study also has other limitations. For instance, hematological disorders were not investigated in relation to acute strokes and malignant ischemic strokes. Gender differences in risk factors, disease types and severity were not considered. To develop more comprehensive and objective research on multidisciplinary refined time management combined with organized stroke management in future studies, we should further expand the scope of the research object and connotation. Therefore, we can provide clinical guidance on acute ischemic stroke treatment.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

LDZ, RN and ZFZ—designed the study and carried them out, LDZ, RN—supervised the data collection, analyzed the data, LDZ, RN—interpreted the data, prepare the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Zhejiang Hospital (Approval no. 2023-4K). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Lingdie Zhao, Rong Niu, Zhufeng Zhang. Effect of multidisciplinary refined time management combined with organized stroke management on the efficacy of intravenous thrombolysis in patients with acute ischemic stroke. Signa Vitae. 2024; 20(3): 81-88. doi: 10.22514/sv.2024.031.