

## Original Article

# Effect of intravenous thrombolysis combined with mechanical thrombectomy on neurological function and short-term prognosis of patients with acute cerebral infarction

Yongchang Liu, Zhen Hong, Yan Li, Shaoquan Li, Qingran Liu, Songwang Xie, Junyong Wang, Jian Wang, Mingming Zheng

*Department of Neurovascular Intervention, Cangzhou Central Hospital, Cangzhou, China*

Received June 1, 2021; Accepted August 9, 2021; Epub April 15, 2022; Published April 30, 2022

**Abstract:** Objective: This study was to assess the effect of intravenous thrombolysis combined with mechanical thrombectomy on neurological function and the short-term prognosis of patients with acute cerebral infarction (ACI). Methods: A total of 120 patients with ACI admitted to our hospital from January 2019 to January 2020 were selected as research objects, and randomized into Group A (n=60) or Group B (n=60). Patients in both groups were treated with intravenous thrombolysis. Group B received ACI conventional treatment and intravenous thrombolysis, while Group A was additionally given mechanical thrombectomy. Then the neurological function scores, serum factor levels, vascular recanalization rate, incidence of adverse reactions, Thrombolysis in Myocardial Infarction (TIMI) grade flow, and effective rate of treatment were compared between the two groups. The clinical trial is available at <https://clinicaltrials.gov/>, ClinicalTrials.gov Identifier: NCT03502411. Results: The neurological function scores of Group A were apparently lower than those of Group B one month after treatment ( $P<0.001$ ). After treatment, Group A yielded a superior serum factor level compared to Group B ( $P<0.001$ ), and also showed a higher recanalization rate of blood vessels and a notably lower adverse reaction rate (all  $P<0.05$ ). Conclusion: Intravenous thrombolysis combined with mechanical thrombectomy can accelerate the recovery of neurological function in patients with ACI, and yield a more promising outcome in terms of the patient's vascular recanalization rate compared with the monotherapy. It can also reduce the adverse reaction rate of patients to ensure a better short-term prognosis.

**Keywords:** Intravenous thrombolysis, mechanical thrombectomy, ACI

## Introduction

ACI is a common clinical disease with a high mortality rate. In many cases, patients who survive from ACI may also be accompanied with serious sequelae, which severely threatens their quality of life [1-3]. With the in-depth research on ACI, vascular thrombosis is basically considered as the cause of ACI in academia, which is indicative of thrombolysis as its treatment method, mainly including intravenous thrombolysis and arterial thrombolysis. Despite the fact that intravenous thrombolysis is appreciated by its simple operation, drug thrombolysis alone fails to deliver an ideal vascular recanalization effect in clinical practice, thus resulting in a poor prognosis of patients [4-7]. In recent years, the upgrading of medical apparatus has yielded more possibilities for

ACI treatment, among which mechanical thrombectomy has become a preferred one with a high vascular recanalization rate and an optimized prognosis. Studies have shown that intravenous thrombolytic therapy before mechanical thrombectomy can increase the recanalization rate of occluded blood vessels in the early stage of ACI, thereby enhancing the effect of neurological function recovery [8-11]. Therefore, this study was to investigate the effect of intravenous thrombolysis combined with mechanical thrombectomy on the neurological function and short-term prognosis of patients with ACI. A total of 120 patients with ACI in our hospital were selected for this research. Ding et al. has previously investigated the hemodynamic changes to explore the effect of arteriovenous thrombolysis combined with mechanical thrombus removal in the treatment of ACI [8]. In this

study, we innovatively used the expression of serum OPN, NT-proBNP, and MDA to evaluate the neurological function of ACI patients after treatment.

### Materials and methods

#### General information

A total of 120 patients with ACI enrolled in our hospital from January 2019 to January 2020 were selected as research objects, and randomized into Group A (n=60) or Group B (n=60). This study was approved by the hospital ethics committee, with an ethics certificate number of 2018-11-15.

#### Inclusion criteria

(1) Patients and their families signed an informed consent form after being fully informed of the research process; (2) Patients were diagnosed with ACI after examination, under the diagnostic criteria of *Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke* [12]; (3) Patients suffered the first onset; (4) The neurological function score was over 4 points [13]; (5) The time from onset to admission was less than 6 hours.

#### Exclusion criteria

(1) Patients with mental problems or unable to have communication; (2) Patients with other organic diseases; (3) Patients with systemic infectious diseases [14]; (4) Patients with allergic physique; (5) Patients with contraindications to intravenous thrombolysis or mechanical thrombectomy [15]; (6) Patients who received surgical treatment within one month before the start of the study.

#### Methods

All patients underwent ACI conventional treatment and intravenous thrombolysis. The specific steps were as follows: (1) The patients were treated with anti-infection, and neurotrophic treatment was given according to their actual conditions to improve their brain blood circulation. (2) The patients were given a 0.9 mg/kg recombinant tissue-type plasminogen activator (Guangzhou Mingkang Bioengineering Co., Ltd., National Medical Products Administration Approval Number: S20150001), with the maximum dose controlled within 90

mg. Moreover, 1/10 of the total dose was injected intravenously in the first 10 minutes, and then the remaining dose was injected within 1 hour. A course of treatment spanned 14 days.

Group A received additional mechanical thrombectomy. The specific steps were as follows: (1) Under local anesthesia, each patient was given femoral artery puncture; with digital subtraction angiography, the tip of a guiding catheter was inserted into the infarct with the guidewire, and the thrombus was removed after the stent was placed. In case of no abnormality, the stent was withdrawn and the artery sheath was removed. (2) The patients' physical data during mechanical thrombectomy were closely monitored to avoid postoperative coma. Five ml of venous blood was drawn and separated; the level of OPN in the serum was measured using the double antibody sandwich method; NT-pro-BNP was measured using ELISA (Shanghai Shenggong); superoxide dismutase (SOD) was measured using Superoxide Dismutase Activity Assay kit (Colorimetric, ab65354); MDA was detected using the end point colorimetric method, and the reacted MDA was determined using TBARS (thiobarbituric acid reactant) technology; its product malondialdehyde dithiobarbituric acid adduct was observed under a spectrophotometer to determine the change of the peak absorbance.

#### Indicators observation

(1) Neurological function score: The patients' scores on the National Institutes of Health Stroke Scale (NIHSS) and the modified RANKIN scale (mRS) were compared. The score is negatively correlated with the patient's neurological function recovery. The comparison time points were before treatment and 1 month after treatment (after treatment) [16, 17].

(2) Serum factor levels: Serum osteopontin (OPN), amino-terminal pro-B-type natriuretic peptide precursor (NT-proBNP), superoxide dismutase (SOD), and malondialdehyde (MDA). The comparison time points were before treatment and 1 month after treatment (after treatment).

(3) Vascular recanalization rate: The rate was evaluated based on the thrombolytic grading system of cerebral infarction. Level 3 was regarded as complete recanalization, level 2 as

## Intravenous thrombolysis for ACI patients

**Table 1.** Comparison of general information of patients

Groups	Cases	Male/female	Age (year)	Onset time (H)	Infarct volume (cm <sup>3</sup> )	Underlying diseases (cases)		
						Hypertension	Coronary Heart Disease	Diabetes
Group A		60	35/25	63.56±5.21	3.54±0.68	4.10±0.65	30	15
Group B		60	36/24	64.21±5.23	3.56±0.87	4.08±0.54	31	14
t/X <sup>2</sup>			0.035	0.682	0.140	0.183	0.033	0.046
P			0.853	0.497	0.889	0.855	0.855	0.831

**Table 2.** Comparison of neurological function scores ( $\bar{x} \pm s$ , points)

Categories	Group A		Group B		t	P-value
NIHSS	Before treatment	17.69±1.94	Before treatment	17.58±1.98	0.307	0.759
	After treatment	7.10±0.65	After treatment	9.87±0.87	19.757	<0.01
	t	40.093	t	27.614		
	P	<0.01	P	0.000		
mRS	Before treatment	4.35±0.65	Before treatment	4.42±0.68	0.576	0.565
	After treatment	2.10±0.31	After treatment	3.15±0.62	11.733	0.000
	t	24.201	t	10.690		
	P	0.000	P	0.000		

partial recanalization, and level lower than 2 as non-recanalization. The comparison time points were before treatment and 1 month after treatment (after treatment).

(4) The incidence of adverse reactions: Adverse reactions include intracranial hemorrhage, urinary tract bleeding, reperfusion injury, and re-vascularization of blood vessels. The number of patients with adverse reactions was recorded. The comparison time points were before treatment and 1 month after treatment (after treatment).

(5) Thrombolysis in Myocardial Infarction (TIMI) grade flow: it was evaluated based on TIMI grade flow. TIMI 0 flow indicates that the diseased segment is occluded without blood perfusion; TIMI 1 flow indicates that the diseased segment can allow the pass of the contrast agent, with an incomplete filling of the blood vessel; TIMI 2 flow refers to delayed or sluggish antegrade flow with complete filling of the vessel; TIMI 3 flow refers to normal flow which fills the vessel completely [18, 19]. The number of patients with adverse reactions was recorded. The comparison time points were before treatment and 1 month after treatment (after treatment).

(6) Effective rate: Recovered: basic disappearance of the patient's clinical symptoms, reduction of the NIHSS score by more than 90%, and

recanalization of blood vessels; Markedly effective: significant alleviation of clinical symptoms, reduction of the NIHSS score by 46%-90%, and vascular recanalization rate greater than 80%; Effective: alleviation of patient's clinical symptoms, reduction of the NIHSS score by 20%-45%, and vascular recanalization rate of 50%-80%; Ineffective: None of above criteria was met. The comparison time points were before treatment and 1 month after treatment (after treatment).

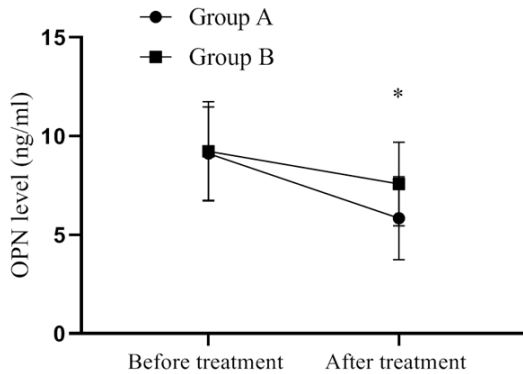
### Statistical analysis

The data processing software selected in this study was SPSS20.0, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used for graphics plotting. The research included count data and measurement data, which were analyzed by X<sup>2</sup> test and t-test, respectively. P<0.05 indicated that the difference was statistically significant.

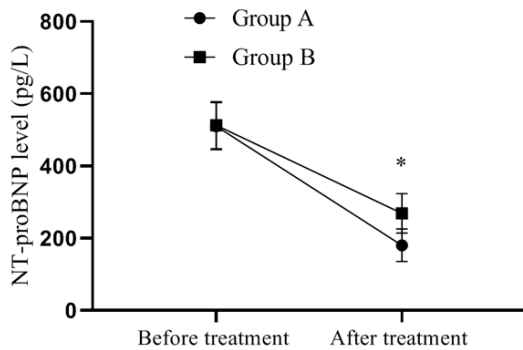
## Results

### Comparison of clinical data

There was no significant difference in gender, age, Onset time, Infarct volume, and Underlying diseases between the two groups (P>0.05). See **Table 1**.



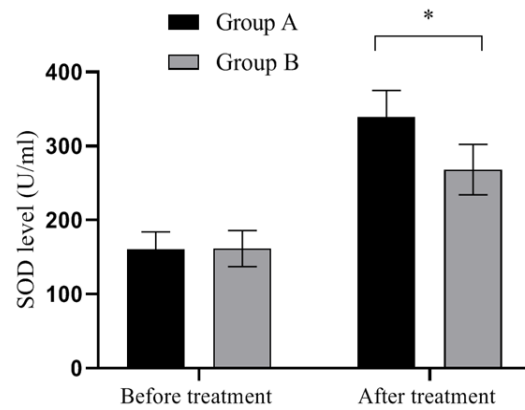
**Figure 1.** Comparison of OPN levels ( $\bar{x}\pm s$ , ng/ml). Notes: In this Figure, the horizontal axis is before and after treatment from left to right, and the vertical axis is OPN level (ng/ml); the dotted line in the figure represents Group A, and the square line represents Group B. The OPN level before treatment in Group A and Group B is (9.12±2.36) ng/ml and (9.23±2.51) ng/ml, respectively, and the comparison results:  $t=0.247$ ,  $P=0.805$ ; The OPN level after treatment in Group A and Group B is (5.84±2.10) ng/ml and (7.58±2.12) ng/ml, respectively, and the comparison results:  $t=4.517$ ,  $P<0.01$ . \* indicates  $P<0.05$ .



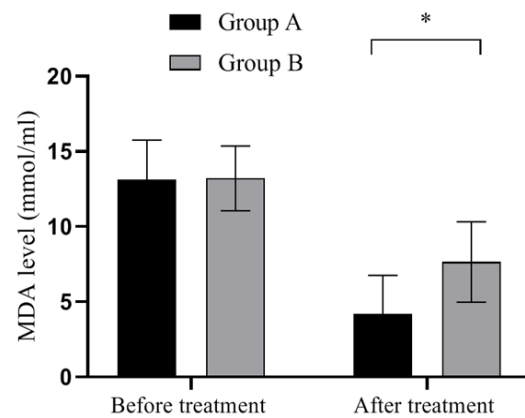
**Figure 2.** Comparison of NT-proBNP levels ( $\bar{x}\pm s$ , pg/L). Note: In this Figure, the horizontal axis is before and after treatment from left to right, and the vertical axis is NT-proBNP level (pg/L); the dotted line in the figure represents Group A, and the square line represents Group B. The NT-proBNP level before treatment in Group A and Group B is (510.65±65.21) pg/L and (512.98±65.29) pg/L, respectively, and the comparison results:  $t=0.196$ ,  $P=0.845$ ; The NT-proBNP level after treatment in Group A and Group B is (180.65±45.11) pg/L and (268.98±54.98) pg/L, respectively, and the comparison results:  $t=9.621$ ,  $P=0.000$ . \* indicates  $P<0.05$ .

#### Comparison of neurological function scores

Before treatment, the NIHSS and mRS scores of both groups were similar ( $P>0.05$ ); after treatment, the NIHSS and mRS scores of both groups were improved compared with before



**Figure 3.** Comparison of SOD levels in patients ( $\bar{x}\pm s$ , U/ml). Note: In this Figure, the horizontal axis is before and after treatment from left to right, and the vertical axis is SOD level (U/ml); the black column in the figure represents Group A, and the gray column represents Group B. The SOD level before treatment in Group A and Group B is (160.65±23.65) U/ml and (161.54±24.21) U/ml, respectively, and the comparison results:  $t=0.204$ ,  $P=0.839$ ; The SOD level after treatment in Group A and Group B is (339.65±35.68) U/ml and (268.15±34.10) U/ml, respectively, and the comparison results:  $t=11.222$ ,  $P=0.000$ . \* indicates  $P<0.05$ .



**Figure 4.** Comparison of MDA levels ( $\bar{x}\pm s$ , mmol/ml). Note: In this Figure, the horizontal axis is before and after treatment from left to right, and the vertical axis is MDA level (mmol/ml); the black column in the figure represents Group A, and the gray column represents Group B. The MDA level before treatment in Group A and Group B is (13.10±2.65) mmol/ml and (13.21±2.15) mmol/ml, respectively, and the comparison results:  $t=0.250$ ,  $P=0.803$ ; The MDA level after treatment in Group A and Group B is (4.21±2.54) mmol/ml and (7.65±2.68) mmol/ml, respectively, and the comparison results:  $t=7.216$ ,  $P=0.000$ . \* indicates  $P<0.05$ .

treatment, with better improvement in Group A ( $P<0.01$ ), as shown in Table 2.

**Table 3.** Comparison of vascular recanalization rate [n (%)]

Groups	Complete recanalization	Partial recanalization	Non-recanalization	Total number of recanalization cases
Group A	30 (50.0)	24 (40.0)	6 (10.0)	54 (90.0)
Group B	24 (40.0)	18 (30.0)	18 (30.0)	42 (70.0)
X <sup>2</sup>	1.212	1.319	7.500	7.500
P	0.271	0.251	0.006	0.006

**Table 4.** Comparison of the incidence of adverse reactions

Group	Intracranial hemorrhage	Urinary tract bleeding	Reperfusion injury	Revascularization	No adverse reactions
Group A	1	1	1	1	56 (93.3)
Group B	2	4	3	5	46 (76.7)
X <sup>2</sup>					6.536
P					0.011

**Table 5.** Comparison of treatment efficiency [n (%)]

Groups	Recovered	Markedly effective	Effective	Ineffective
Group A	24 (40.0)	28 (46.7)	5 (8.3)	3 (5.0)
Group B	12 (20.0)	18 (30.0)	15 (25.0)	15 (25.0)
X <sup>2</sup>	6.316	10.439	0.000	9.701
P	0.012	0.001	1.000	0.002

#### Comparison of serum factor levels

Before treatment, the two groups showed no obvious disparity in OPN, NT-proBNP, SOD, and MDA levels ( $P>0.05$ ). After treatment, Group A yielded lower levels of OPN, NT-proBNP, and MDA, and a higher level of SOD than Group B. Superior results of serum factor levels in Group A compared with Group B were found ( $P<0.001$ ). See **Figures 1-4**.

#### Comparison of vascular recanalization rate

The total recanalization rate in Group A was 90%, which was higher than that of 70.0% in Group B ( $P=0.006$ ). See **Table 3**.

#### Comparison of the incidence of adverse reactions

In Group A, we observed 1 case of intracranial hemorrhage, 1 case of urinary tract bleeding, 1 case of reperfusion injury, 1 case of revascularization, and 56 cases without adverse reactions. In Group B, we observed 2 cases of intracranial hemorrhage, 4 cases of urinary tract

bleeding, 3 cases of reperfusion injury, 5 cases of revascularization, and 46 cases without adverse reactions. Patients in Group A enjoyed a lower adverse reaction rate than patients in Group B ( $P=0.011$ ). See **Table 4**.

#### Comparison of treatment efficiency

**Table 5** demonstrates that Group A yielded a more promising ineffective rate than Group B (5% vs. 25.0%  $P<0.05$ ).

#### Discussion

Intravenous thrombolysis can improve the state of blood supply to the brain of patients with ACI, which enhances the metabolism of brain tissue and thus ensures a further recovery of brain nerve cells. The recombinant tissue-type plasminogen activator selected in the study is a common clinical treatment drug. It can accelerate the degradation of fibrin at the cerebral infarction, optimize the blood circulation in the infarct, and restore the normal oxygen supply [20-22]. The brain treatment of patients with ACI has been initially visualized, and arterial catheter intervention has become one of the frequently used clinical treatment methods for ACI. Compared with conventional thrombolytic therapy, mechanical thrombectomy can help directly achieve vascular recanalization by removing the thrombus, thus ensuring a higher postoperative vascular recanalization rate, as compared to single thrombolytic therapy. Moreover, this treatment method can lower the possibility of incomplete removal of thrombus, which guarantees a better short-term prognosis. This study revealed a higher vascular recanalization rate and TIMI grade flow of Group A than those of Group B (both  $P<0.05$ ), indicating that combination therapy can improve vascular recanalization rate in patients with ACI and restore blood supply to the brain. The lower neurological function scores of Group A compared with those of Group B ( $P<0.001$ ) one month after treatment were attributed to sufficient nutrient supply to the glial cells after the restoration of blood supply, which maximizes the recovery of neurological function.



The study also found that the serum factor levels of Group A after treatment were significantly better than those of Group B ( $P < 0.001$ ). Among them, OPN was positively correlated with the neurological function score of patients with ACI. This extracellular matrix component of nerve tissue is highly sensitive to brain nerve injury and thus can be used to evaluate the prognosis of patients. Furthermore, NT-proBNP will flood into the blood after nerve damage in patients with ACI. Its level has been confirmed to be in a downward trend in the body of patients with ACI after thrombolytic therapy, indicating a close relationship between NT-proBNP and the treatment efficiency of the patient. In addition, oxidative stress gives rise to a decline in the patient's nerve function. As the final product of oxidative stress, MDA hence can reflect the peroxidative damage in the patient's body, and SOD is a protective factor that eliminates oxygen free radicals; As a result, both of them show great potential in the prognostic evaluation for patients with ACI [23, 24]. A more promising outcome of the above indicators in Group A demonstrated that mechanical thrombectomy combined with intravenous thrombolysis can optimize the secretion of nerve function-related factors and mitigate oxidative stress, thus accelerating the recovery of nerve function and reducing the damage to brain tissue [25].

The incidence of adverse reactions in Group A was significantly lower than that in Group B ( $P < 0.05$ ), which was consistent with the research results reported by Zhao et al. [26]. In their study, the mechanical thrombectomy combined with thrombolytic therapy yields a better effect than single treatment in the treatment of moderate to severe ACI, with a similar incidence of adverse reactions, suggesting the high safety of the therapy. The limitation of this study lies in the absence of long-term follow-up and statistics on the long-term survival rate and disease progression-free survival time of patients in Group A, which should be improved in future studies.

In conclusion, intravenous thrombolysis combined with mechanical thrombectomy can accelerate the recovery of neurological function in patients with ACI, and yield a more promising outcome in terms of the patient's vascular recanalization rate and TIMI grade flow than monotherapy. It can also reduce the adverse

reaction rate to ensure a better short-term prognosis.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Yongchang Liu, Department of Neurovascular Intervention, Cangzhou Central Hospital, Cangzhou, China. Tel: +86-1339-3276256; E-mail: liuyongchang2021@126.com

## References

- [1] Katano T, Sakamoto Y, Kunugi S, Nishiyama Y, Shimizu A and Kimura K. A fungus in a thrombus by mechanical thrombectomy in acute cerebral infarction: a case report. *Rinsho Shinkeigaku* 2020; 60: 340-345.
- [2] Janssen H, Brückmann H, Killer M, Heck S, Buchholz G and Lutz J. Acute basilar thrombosis: recanalization following intravenous thrombolysis is dependent on thrombus length. *PLoS One* 2018; 13: e0193051.
- [3] Prochazka V, Jonszta T, Czerny D, Krajca J, Roubec M, Macak J, Kovar P, Kovarova P, Pulcer M, Zoubkova R, Lochman I, Svachova V, Pavliska L, Vrtkova A, Kasprak D, Gumulec J and Weisel JW. The role of von willebrand factor, ADAMTS13, and cerebral artery thrombus composition in patient outcome following mechanical thrombectomy for acute ischemic stroke. *Med Sci Monit* 2018; 24: 3929-3945.
- [4] Funatsu N, Hayakawa M, Hashimoto T, Yamagami H, Satow T, Takahashi JC, Koga M, Nagatsuka K, Ishibashi-Ueda H, Iwama T and Toyoda K. Vascular wall components in thrombi obtained by acute stroke thrombectomy: clinical significance and related factors. *J Neurointerv Surg* 2019; 11: 232-236.
- [5] Hashimoto T, Hayakawa M, Funatsu N, Yamagami H, Satow T, Takahashi JC, Nagatsuka K, Ishibashi-Ueda H, Kira JI and Toyoda K. Histopathologic analysis of retrieved thrombi associated with successful reperfusion after acute stroke thrombectomy. *Stroke* 2016; 47: 3035-3037.
- [6] Szuchy Kristiansen E, Holm Vestergaard H, Modrau B and Oppel LM. Acute ischemic stroke in late pregnancy treated with intravenous thrombolysis and endovascular therapy. *Case Rep Neurol* 2019; 11: 41-46.
- [7] De Meyer SF, Andersson T, Baxter B, Bendszus M, Brouwer P, Brinjikji W, Campbell BC, Costalat V, Dávalos A, Demchuk A, Dippel D, Fiehler J, Fischer U, Gilvarry M, Gounis MJ, Gralla J, Jansen O, Jovin T, Kallmes D, Khatri P, Lees KR, López-Cancio E, Majoie C, Marquering H, Narata AP, Nogueira R, Ringleb P, Siddiqui A, Szikora I, Vale D, von Kummer R, Yoo AJ, Hacke

- W and Liebeskind DS; Clot Summit Group. Analyses of thrombi in acute ischemic stroke: a consensus statement on current knowledge and future directions. *Int J Stroke* 2017; 12: 606-614.
- [8] Ding T, Tang L, Hu B, Yuan J, Li X and Wen J. Effects of arteriovenous thrombolysis combined with mechanical thrombectomy on efficacy and neurological function of acute cerebral infarct patients. *Biomed Res Int* 2020; 2020: 9743075.
- [9] Marto JP, Kauppila LA, Jorge C, Calado S, Viana-Baptista M, Pinho-E-Melo T and Fonseca AC. Intravenous thrombolysis for acute ischemic stroke after recent myocardial infarction: case series and systematic review. *Stroke* 2019; 50: 2813-2818.
- [10] Khilchuk AA, Vlasenko SV, Scherbak SG, Sarana AM and Popov VV. Successful carotid thrombus aspiration, middle cerebral mechanical thrombectomy, and axillary artery clot disruption attempt in a patient with acute ischemic stroke and critical upper limb ischemia. *Radiol Case Rep* 2017; 13: 183-185.
- [11] El Nawar R, Yeung J, Labreuche J, Chadenat ML, Duong DL, De Malherbe M, Cordoliani YS, Lapergue B and Pico F. MRI-based predictors of hemorrhagic transformation in patients with stroke treated by intravenous thrombolysis. *Front Neurol* 2019; 10: 897.
- [12] Lin YH, Lou M, Zhu RY, Yan YQ, Zhen ZC and Ding MP. Multi-mode MRI-based intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) reduces hemorrhagic transformation in ischemic stroke patients. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 2012; 41: 665-671.
- [13] Suzuki K, Matsumaru Y, Takeuchi M, Morimoto M, Kanazawa R, Takayama Y, Kamiya Y, Shigeta K, Okubo S, Hayakawa M, Ishii N, Koguchi Y, Takigawa T, Inoue M, Naito H, Ota T, Hirano T, Kato N, Ueda T, Iguchi Y, Akaji K, Tsuruta W, Miki K, Fujimoto S, Higashida T, Iwasaki M, Aoki J, Nishiyama Y, Otsuka T and Kimura K; SKIP Study Investigators. Effect of mechanical thrombectomy without vs with intravenous thrombolysis on functional outcome among patients with acute ischemic stroke: the SKIP randomized clinical trial. *JAMA* 2021; 325: 244-253.
- [14] Okamura K, Kodaka M, Ichikawa J, Ando K and Komori M. Left atrial thrombus formation within a few days of hospitalization in semi-acute ischemic heart disease despite no atrial fibrillation and mitral stenosis: a case report. *JA Clin Rep* 2020; 6: 86.
- [15] Lee BY, Oh JS and Yoon SM. Long-term prognosis of patients who contraindicated for intravenous thrombolysis in acute ischemic stroke. *J Cerebrovasc Endovasc Neurosurg* 2019; 21: 77-85.
- [16] Aizawa Y, Nakai T, Saito Y, Monno K, Morikawa T, Kogawa R, Hatta T, Tamaki T, Kato M, Arimoto M, Osaka S, Sunagawa K, Tang XY, Tanaka M, Hao H and Hirayama A. Calcified amorphous tumor-induced acute cerebral infarction. *Int Heart J* 2018; 59: 240-242.
- [17] Choi JI, Ha SK, Lim DJ, Kim SD and Kim SH. S100 $\beta$ , matrix metalloproteinase-9, D-dimer, and heat shock protein 70 are serologic biomarkers of acute cerebral infarction in a mouse model of transient MCA occlusion. *J Korean Neurosurg Soc* 2018; 61: 548-558.
- [18] Nakamura Y, Nakajima H, Kimura F, Unoda K and Arawaka S. Preventive effect of cilostazol on pneumonia in patients with acute cerebral infarction. *J Stroke Cerebrovasc Dis* 2018; 27: 2354-2359.
- [19] Osawa A, Maeshima S and Tanahashi N. Efficacy of cilostazol in preventing aspiration pneumonia in acute cerebral infarction. *J Stroke Cerebrovasc Dis* 2013; 22: 857-861.
- [20] Aizawa Y, Nakai T, Saito Y, Monno K, Morikawa T, Kogawa R, Hatta T, Tamaki T, Kato M, Arimoto M, Osaka S, Sunagawa K, Tang XY, Tanaka M, Hao H and Hirayama A. Calcified amorphous tumor-induced acute cerebral infarction. *Int Heart J* 2018; 59: 240-242.
- [21] Popovic P, Popovic V, Schaffer R and Sutton CH. Treatment of experimental cerebral infarction in rats with levodopa or with glycerol. *J Neurosurg* 1978; 48: 962-969.
- [22] Siri SRA, Eliassen BM, Jacobsen BK, Melhus M, Broderstad AR, Michalsen VL and Braaten T. Changes in conventional cardiovascular risk factors and the estimated 10-year risk of acute myocardial infarction or cerebral stroke in Sami and non-Sami populations in two population-based cross-sectional surveys: the SAMINOR study. *BMJ Open* 2019; 9: e028939.
- [23] Siri SRA, Braaten T, Jacobsen BK, Melhus M and Eliassen BM. Distribution of risk factors for cardiovascular disease and the estimated 10-year risk of acute myocardial infarction or cerebral stroke in Sami and non-Sami populations: the SAMINOR 2 clinical survey. *Scand J Public Health* 2018; 46: 638-646.
- [24] Deguchi I, Osada T and Takao M. Prescription status of oral anticoagulants in patients with acute cerebral infarction with non-valvular atrial fibrillation at the time of stroke onset. *J Cardiol* 2020; 75: 544-548.
- [25] Kitajima A, Otsuka Y, Lefor AK and Sanui M. Acute cerebral infarction in a patient with an epidural catheter after left upper lobectomy: a case report. *BMC Anesthesiol* 2019; 19: 27.
- [26] Zhao QS, Li W, Li D, Liu T, Wang JH, Gao Y, Yi L and Zhao RK. Clinical treatment efficiency of mechanical thrombectomy combined with rh-Pro-UK thrombolysis for acute moderate/severe cerebral infarction. *Eur Rev Med Pharmacol Sci* 2018; 22: 5740-5746.