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ARTICLE

Effect of Tirofiban on Cognitive Function in Patients With Unruptured Intracranial Aneurysms After Endovascular Embolization

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Abstract

Aims/Background An unruptured intracranial aneurysm (UIA) is a cerebrovascular disease with a potential risk of rupture. Rupture of UIA is a leading cause of spontaneous subarachnoid hemorrhage, which carries a high mortality rate. While endovascular intervention emerged as the primary treatment option for UIA, postoperative cognitive dysfunction (POCD) remains a common complication, affecting patients' postoperative recovery. Therefore, identifying effective interventions is clinically crucial for improving postoperative cognitive function. Tirofiban, an antiplatelet agent, has shown potential neuroprotective effects in neurointerventional procedures. Hence, this study aims to evaluate the effect of tirofiban on postoperative cognitive function in patients with UIA.

Methods This retrospective study analyzed 125 UIA patients who underwent treatment between January 2021 and December 2024. All patients underwent simple coil embolization and were divided into two groups: an observation group (treated with tirofiban) and a control group (without tirofiban). Before surgery, these patients were routinely treated with aspirin and clopidogrel. However, patients in the observation group were given tirofiban in addition to standard care for 12 hours after the procedure. Furthermore, cognitive function was assessed before and after surgery using the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) scores. Additionally, the incidence of postoperative silent cerebral infarction (SCI) and variations in inflammatory marker levels were compared between the two groups.

Results Cognitive function showed no significant difference between the two groups before surgery. After the procedure, the observation group demonstrated significantly higher MoCA ($p < 0.001$) and MMSE ($p = 0.001$) scores than the control group, indicating a significant advantage of tirofiban in improving cognitive function. Within 72 hours postoperatively, 7 cases in the observation group developed SCI compared to 18 cases in the control group, with a significantly lower incidence of SCI in the observation group ($p = 0.025$). Preoperative comparison of inflammatory markers revealed no difference between the two groups ($p > 0.05$). However, their postoperative levels were significantly lower in the observation group ($p < 0.05$). The cognitive function scores remained significantly higher in the observation group than in the control group over one month follow-up period ($p < 0.05$).

Conclusion Tirofiban improves cognitive function and reduces SCI and inflammation following UIA embolization, possibly via antiplatelet and anti-inflammatory mechanisms. While statistically significant, the clinical relevance of cognitive improvement (1 point) is limited and requires further investigation. Furthermore, prospective randomized trials are needed to validate the long-term efficacy of tirofiban and elucidate underlying mechanisms.

Key words: intracranial aneurysm; cognition disorders; tirofiban; cerebral infarction; inflammation; endovascular procedures

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Introduction

An unruptured intracranial aneurysm (UIA) is a localized, pathological dilation of the intracranial arterial wall that carries a potential risk of rupture. With increased public awareness about stroke prevention and the widespread use of noninvasive imaging techniques such as magnetic resonance angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA), the detection rate of unruptured intracranial aneurysm (UIA) has increased significantly, with a prevalence of approximately 1% to 7% in the general population (Thien et al, 2017). The rupture of a UIA is the primary cause of spontaneous subarachnoid hemorrhage (SAH), a condition associated with a poor prognosis and a mortality rate reaching 50% (Juvela, 2019; Hoh et al, 2023). Therefore, proactive preventive management of UIA holds significant clinical importance.

Currently, the primary treatment options for UIA include craniotomy and endovascular intervention. Compared to traditional craniotomy, endovascular intervention is considered safer due to its less direct trauma to the cerebrovascular system (Molyneux et al, 2005). In recent years, with continuous advancements in interventional materials and techniques, endovascular intervention has gradually become the preferred treatment option for UIA (Fargen et al, 2018). However, postoperative cognitive dysfunction (POCD) remains a prevalent neurological complication following endovascular treatment of UIA. Clinically, it is manifested as cognitive decline, memory impairment, reduced judgment, and other symptoms like anxiety or confusion (Varpaei et al, 2024). Evidence indicates that endovascular treatment for UIA may lead to significant postoperative cognitive impairment (International Study of Unruptured Intracranial Aneurysms Investigators, 1998). For instance, a study by Kang et al (2013), reported a 44% incidence of POCD within one week postoperatively among 40 patients. POCD not only affects postoperative recovery but also prolongs hospital stays and increases readmission and mortality rates (Eldehni and McIntyre, 2012). Therefore, preventing and improving POCD in UIA patients is of critical clinical significance for improving patient outcomes.

Tirofiban is a highly selective small-molecule antagonist of the glycoprotein IIb/IIIa (GP IIb/IIIa) receptor, known for its potent antiplatelet activity. It has been widely used in the management of acute coronary syndrome and during percutaneous coronary interventions (PCI) (Zhao et al, 2024). In recent years, its application in endovascular treatment for ischemic stroke has increased. By inhibiting thrombus formation and improving cerebral blood flow, tirofiban has been proven to reduce the risk of neurological deterioration (Zhao et al, 2024). Given these potential neuroprotective benefits, this study aims to evaluate the effect of tirofiban on cognitive function in patients after endovascular intervention for UIA, providing new interventional strategies and evidence-based guidance for postoperative management.

Methods

Selection of Study Subjects

This retrospective study collected data from 125 UIA patients admitted to the Department of Neurosurgery, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China, between January 2021 and December 2024. The study was approved by the hospital's Ethics Committee (Approval No. 20254 90101) and was conducted following the principles outlined in the Declaration of Helsinki.

The inclusion criteria for patient selection were as follows:

(1) Individuals aged between 18 and 75 years with normal cognitive function before surgery;

(2) Individuals with diagnosis of UIA with an aspect ratio (dome-to-neck ratio) $\geq$2, and treated with simple coil embolization under general anesthesia;

(3) Individuals with complete clinical data;

(4) Individuals providing informed consent.

The exclusion criteria were as follows:

(1) Individuals with history of thrombocytopenia or coagulation dysfunction;

(2) Pregnant or lactating women;

(3) Individuals with severe comorbidities such as malignant hypertension, chronic liver failure, or psychiatric conditions;

(4) Individuals with history of brain surgery;

(5) Individuals with known contraindications to tirofiban.

Grouping of Study Participants and Treatment Protocol

Study participants (n = 125) were divided into the control and observation groups based on whether tirofiban was administered. The control group received standard preoperative antiplatelet therapy comprising aspirin and clopidogrel, while the observation group received tirofiban at a dose of 0.1 μg/(kg·min) for 12 hours postoperatively, in addition to the standard antiplatelet therapy.

Both groups underwent simple coil embolization. Antiplatelet therapy was initiated 3 to 5 days before surgery, with patients receiving oral doses of 100 mg aspirin and 75 mg clopidogrel. After inducing general anesthesia, an 8F arterial sheath was inserted into the right femoral artery using the Seldinger technique. A guiding catheter of appropriate diameter was then introduced through the arterial sheath and positioned at the C2 segment of the internal carotid artery. Under X-ray guidance, complete cerebral angiography was performed to visualize the target vessel. Multidirectional, three-dimensional imaging was used to thoroughly assess the anatomical relationship between UIA and adjacent vessels. The size of the UIA and the dome-to-neck ratio were measured intraoperatively via angiography to guide the procedure. However, detailed measurements of size and location were not recorded for subsequent analysis.

After systemic heparinization, simple coil embolization was performed. A microcatheter, pre-shaped according to the morphology of the UIA, was inserted into the aneurysm sac under the guidance of a neuro-microguidewire using the work-

ing roadmap. Coils of appropriate diameter, length, and flexibility were selected based on the aneurysm's size and deployed into the aneurysm sac to form a basket-like structure. After confirming the proper positioning through an angiography, the coils were detached. Additional coils were inserted sequentially until the aneurysm sac was densely filled. Post-embolization angiography was then performed to assess the completeness of the embolization and to ensure sufficient blood flow in the parent artery.

Observation Indicators

Cognitive Function Assessment

Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) (Nasreddine et al, 2005; Jia et al, 2021). These evaluations were performed both before and 72 hours after surgery. Both the MoCA and MMSE have a total score of 30 points, with lower scores indicating more severe cognitive impairment. To minimize bias, assessments were conducted by independent evaluators blinded to the patient's group assignments.

Comparison of Inflammatory Markers

Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels were determined using an enzyme-linked immunosorbent assay (ELISA). Peripheral venous blood samples (3 mL) were collected before surgery and again 72 hours postoperatively. C-reactive protein (CRP) levels and neutrophil counts were measured using peripheral venous blood samples (5 mL) collected before surgery and at 72 hours postoperatively.

Incidence of Silent Cerebral Infarction (SCI)

Within 72 hours post-surgery, SCI was assessed using diffusion weighted imaging (DWI) of the brain. SCI was defined as a newly appearing hyperintense lesion of $\geq$3 mm in diameter on the postoperative DWI without any corresponding focal neurological symptoms or signs (Gupta et al, 2016; Conen et al, 2019; Chaturvedi et al, 2023). The images were independently evaluated in a double-blind manner by two neuroradiologists. However, lesions smaller than 3 mm and imaging artifacts were excluded from the final analysis. Figs. 1,2 show representative imaging findings.

Data Analysis

Sample Size Consideration

This study used a retrospective design and included 125 UIA patients who met the inclusion criteria between January 2021 and December 2024. To assess the statistical power of the sample size, the postoperative MoCA scores were used as the primary outcome measure. The calculated effect size between the observation group (26.50 $\pm$ 1.78) and the control group (24.82 $\pm$ 2.20) was 0.84. Using G*Power software (version 3.1.9.7, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) with a significance level of α = 0.05 (two-tailed), the statistical power was determined to be 0.99. Statistical power exceeds the conventional

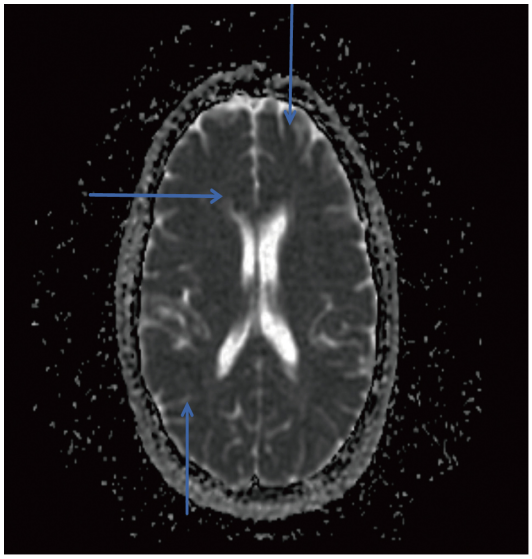

Fig. 1. MRI-ADC sequence of asymptomatic cerebral infarction. Blue arrows indicate regions of restricted diffusion associated with silent cerebral infarction, as identified on ADC mapping. MRI, Magnetic Resonance Imaging; ADC, Apparent Diffusion Coefficient.

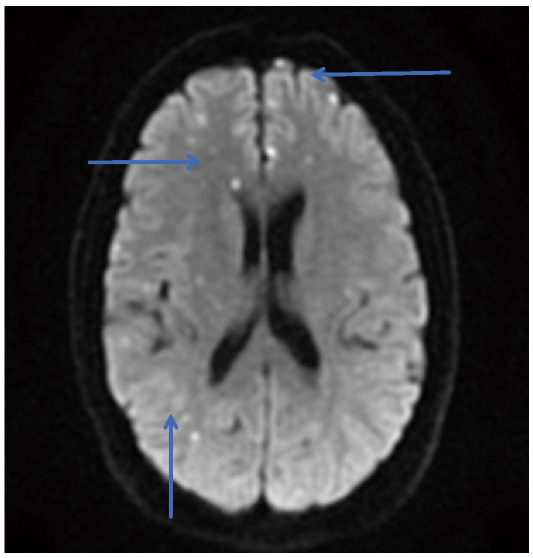

Fig. 2. MRI-DWI sequence of asymptomatic cerebral infarction. Blue arrows indicate regions of restricted diffusion associated with silent cerebral infarction, as identified on ADC mapping. DWI, diffusion weighted imaging.

threshold of 0.80, indicating that the sample size was sufficient to detect significant differences in the primary outcome.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to examine the normality of continuous variables. Those following normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared between groups using an independent sample *t*-test (e.g., MoCA and MMSE scores), while within-group comparisons were conducted

Table 1. Comparison of baseline characteristics between the two groups.

Variable	Total (n = 125)	Observation group (n = 60)	Control group (n = 65)	t/χ^2	*p*-value
Gender				0.031	0.861
Male	51 (40.80%)	24 (40.00%)	27 (41.54%)		
Female	74 (49.20%)	36 (60.00%)	38 (58.46%)		
Age (years)	63.10 ± 10.74	63.22 ± 11.37	63.0 ± 10.21	0.112	0.911
BMI (kg/m^2)	23.75 ± 2.24	23.61 ± 2.39	23.87 ± 2.10	0.630	0.530
Smoking				0.449	0.503
Yes	28 (22.40%)	15 (25.00%)	13 (20.00%)		
No	97 (77.60%)	45 (75.00%)	52 (80.00%)		
Alcohol				1.534	0.216
Yes	29 (23.20%)	11 (18.33%)	18 (27.69%)		
No	96 (76.80%)	49 (81.67%)	47 (72.31%)		
Family history				0.770	0.380
Yes	33 (26.40%)	18 (30.00%)	15 (23.08%)		
No	92 (73.60%)	42 (70.00%)	50 (76.92%)		
Hypertension				$\chi^2 = 0.860$	0.354
Yes	53 (42.40%)	28 (46.67%)	25 (38.46%)		
No	72 (57.60%)	32 (53.33%)	40 (61.54%)		
Diabetes mellitus				$\chi^2 = 0.469$	0.493
Yes	38 (30.40%)	20 (33.33%)	18 (27.69%)		
No	87 (69.60%)	40 (66.67%)	47 (72.31%)		
Heart disease				$\chi^2 = 0.167$	0.683
Yes	14 (11.20%)	6 (10.00%)	8 (12.31%)		
No	111 (88.80%)	54 (90.00%)	57 (87.69%)		

Data are presented as mean ± standard deviation ($\bar{x} \pm s$) or frequency (percentage, %). Age and body mass index (BMI) were compared between groups using the independent samples *t*-test; gender, smoking, alcohol use, and family history were compared using the χ^2 test. $p < 0.05$ indicates statistical significance.

Table 2. Comparison of cognitive function between the two groups.

	MoCA		MMSE	
	Preoperative	Postoperative 72 h	Preoperative	Postoperative 72 h
Observation group (n = 60)	27.12 ± 1.69	26.50 ± 1.78	28.08 ± 1.42	27.53 ± 2.00
Control group (n = 65)	27.01 ± 1.68	24.82 ± 2.20	28.35 ± 1.18	26.25 ± 2.39
t	0.336	4.682	1.155	3.281
p-value	0.738	<0.001	0.251	0.001

Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) were compared using the *t*-tests; $p < 0.05$ indicates statistical significance.

employing a paired sample *t*-test. Non-normally distributed data were expressed as median (interquartile range) and analyzed using the Mann-Whitney U test (e.g., CRP, IL-6, TNF-α). Categorical data were expressed as frequencies (percentage, %) and compared using the chi-square test (e.g., SCI incidence). A *p*-value < 0.05 was considered statistically significant.

Table 3. Results of multivariate regression analysis.

Outcomes	Variable	β	SE	t/Wald	β/OR	95% CI	p-value
MMSE	Tirofiban	/	0.40	3.26	1.29	0.51–2.06	0.001
MoCA	Tirofiban	/	0.36	4.68	1.68	0.98–2.39	<0.001
SCI	Tirofiban	–1.06	0.49	4.75	0.34	0.13–0.90	0.029

MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; SCI, silent cerebral infarction; CI, confidence intervals; OR, odds ratios.

To account for the effects of potential confounding factors, multivariable analyses were conducted for key outcomes, including postoperative MoCA scores, MMSE scores, and SCI incidence. Findings were reported as regression coefficients (β) or odds ratios (OR), along with their corresponding 95% confidence intervals (CI). A p-value of <0.05 was considered statistically significant.

Results

Comparison of Baseline Characteristics Between the Two Groups

Out of the total 125 UIA patients, 60 individuals received tirofiban therapy. There were no significant differences in baseline characteristics between the two groups (Table 1).

Comparison of Cognitive Function Between the Two Groups

There were no significant differences in baseline cognitive function between the control and observation groups before surgery ($p > 0.05$). However, both MMSE ($p = 0.001$) and MoCA ($p < 0.001$) scores significantly declined in the control groups after surgery, while the observation group showed a postoperative decline in MMSE ($p = 0.001$) and MoCA ($p = 0.002$) scores. However, this decline was less pronounced. Postoperative comparison between the two groups revealed that the observation group had significantly higher cognitive scores than the control group, with statistically significant differences in MMSE ($p = 0.001$) and MoCA ($p < 0.001$) (Table 2). In the multivariable linear regression analysis, after adjusting for sex, hypertension, diabetes, heart disease, smoking history, alcohol consumption, family history, age, and body mass index (BMI), the postoperative MoCA and MMSE scores remained significantly higher in the observation group (Table 3). These results indicate that the cognitive improvements associated with tirofiban administration are independent of these confounding factors.

Comparison of Inflammatory Markers Between the Two Groups

No significant differences in preoperative inflammatory marker levels were observed between the control and observation groups. At 72 hours postoperatively, levels of neutrophils, CRP, TNF-α, and IL-6 were significantly lower in the observation group compared to the control group (Table 4).

Comparison of Silent Cerebral Infarction

In the observation group, 7 cases developed SCI postoperatively, compared to 18 cases in the control group. The incidence of SCI was significantly lower in the observation group than in the control group (Table 5). In the multivariable logistic regression analysis, after adjusting for sex, hypertension, diabetes, heart disease, smoking history, alcohol consumption, family history, age, and BMI, the incidence of SCI was significantly lower in the observation group compared to the control group (OR = 0.34, 95% CI: 0.13–0.90, $p = 0.029$). These results suggest that the neuroprotective effect of tirofiban is independent of these potential confounding factors (Table 3).

Follow-Up

At 1 month postoperatively, cognitive function was reassessed in both groups. The observation group showed MoCA and MMSE scores of 27.05 ± 1.55 and 27.98 ± 1.31, respectively, while the control group had scores of 26.28 ± 2.32 and 26.82 ± 1.57, respectively. Statistically significant differences were observed between the two groups for both MoCA ($t = 2.177$, $p = 0.031$) and MMSE ($t = 4.498$, $p < 0.001$).

Discussion

The results of this study revealed significantly higher postoperative MMSE and MoCA scores in patients treated with tirofiban compared to those who did not receive it, indicating that tirofiban may offer potential advantages in improving postoperative cognitive function. However, while the observed improvement, approximately 1 point on both the MoCA and MMSE, was statistically significant ($p < 0.001$ and $p = 0.001$), its clinical significance remains uncertain. The minimal clinically important difference (MCID) for MoCA and MMSE ranges from 1.5–2 points in populations with neurodegenerative diseases (Andrews et al, 2019; Wu et al, 2019). Although no specific MCID has been established for UIA patients, the observed improvement in our study may not exceed that threshold, suggesting limited clinical impact. Therefore, the conclusions of this study have been cautiously tempered to reflect this limitation.

Elderly patients with UIA often experience cognitive decline after treatment, with long-term alleviation in overall cognitive function often exceeding executive function (Sakurada et al, 2024). The specific mechanisms underlying cognitive dysfunction after endovascular treatment for UIA remain unclear, but thrombus formation and subsequent dislodgement are considered possible reasons. New-onset cerebral infarctions after intracranial aneurysm embolization are primarily attributed to embolus dislodgement. Thrombus formation may result from fresh thrombi developed by coil packing, the dislodgement of pre-existing thrombi, or the overuse of coils leading to protrusion into the parent artery (Schacht et al, 2020). Furthermore, guidewire stimulation can provoke vascular spasms and microthrombus formation, while vascular injury can lead to postoperative cortical infarction, both of which contribute to cognitive dysfunction (Meila et al, 2015).

Table 4. Comparison of inflammatory markers between two groups before and after surgery.

	CRP		Neutrophils		TNF-α		IL-6	
	Preoperative	Postoperative 72 h	Preoperative	Postoperative 72 h	Preoperative	Postoperative 72 h	Preoperative	Postoperative 72 h
Control group (n = 65)	3.20 (2.20, 6.50)	6.80 (5.50, 9.40)	4.70 (2.50, 6.50)	6.30 (5.30, 7.90)	5.80 (2.90, 7.80)	5.90 (4.70, 9.60)	5.40 (3.20, 6.80)	6.50 (5.60, 7.80)
Observation group (n = 60)	3.20 (2.05, 5.98)	5.30 (4.65, 6.05)	4.65 (2.65, 6.35)	5.70 (4.97, 6.80)	5.80 (2.70, 7.80)	5.70 (3.77, 6.50)	5.30 (3.18, 6.73)	4.80 (3.32, 7.00)
Z	–0.67	–4.14	–0.05	–2.05	–0.11	–2.15	–0.14	–3.58
p-value	0.503	<0.001	0.961	0.040	0.911	0.032	0.886	<0.001

C-reactive protein (CRP) and interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) were compared using the Mann-Whitney U tests; $p < 0.05$ indicates statistical significance.

Table 5. Comparison of silent cerebral infarction incidence between the two groups.

	Observation group (n = 60)	Control group (n = 65)	χ^2	*p*-value
New-onset SCI			5.008	0.025
Yes	7 (11.67%)	18 (27.69%)		
No	53 (88.33%)	47 (72.31%)		

Silent cerebral infarction (SCI) was compared using the χ^2 tests, $p < 0.05$ indicates statistical significance.

Thrombus dislodgement is a well-recognized high-risk factor in intracranial aneurysm interventional therapy. Through its antiplatelet aggregation effect, tirofiban can effectively reduce microthrombus dislodgement during interventional therapy, thereby decreasing the thrombotic burden within cerebral arteries. Furthermore, by inhibiting platelet aggregation, tirofiban may indirectly reduce local vascular inflammatory and stress responses within intracranial arteries (Walters et al, 2010). More importantly, tirofiban reduces the risk of distal embolism, improves cerebral microcirculation, enhances reperfusion in infarcted areas, and alleviates ischemic brain injury (Kim et al, 2017). These mechanisms may likely contribute to the protective effect of tirofiban on postoperative cognitive function. A study investigated the neuroprotective effects of tirofiban in patients with acute ischemic stroke (AIS) by reducing inflammatory responses. The findings revealed that tirofiban significantly reduced cerebral infarct volume in a mouse model of AIS and improved neurological outcomes by modulating microglial activation and decreasing the levels of inflammatory cytokines (Liu et al, 2024). Additionally, Yingdao Chen and colleagues (2025) demonstrated that combining tirofiban with neurointerventional therapy improved neurological function and positively impacted electroencephalogram (EEG) parameters on neurological function and indicators in patients with cerebral infarction. A multicenter study further confirmed that tirofiban reduced the risk of early neurological deterioration in non-cardioembolic stroke patients presenting within 24 hours of onset without increasing the risk of symptomatic intracranial or systemic hemorrhage (Zhao et al, 2024). Furthermore, tirofiban showed a favorable safety profile in AIS patients receiving intravenous thrombolytic therapy (Shi et al, 2023).

Our study observed that, compared to patients who did not receive tirofiban, those treated with tirofiban showed significantly lower postoperative neutrophil counts, CRP, and TNF-α levels, as well as improved postoperative MoCA and MMSE scores. These results suggest that tirofiban may enhance cognitive function by regulating the inflammatory response. Xiang and colleagues (2025) investigated prognostic risk factors associated with anticoagulant therapy in patients undergoing endovascular treatment for UIAs and found that tirofiban reduced the incidence of embolic events without increasing the risk of hemorrhage.

Furthermore, our study found that tirofiban improved cognitive function within 72 hours postoperatively, aligning with previous findings (Zhao et al, 2024); however, unlike prior investigations, this study specifically targeted UIA patients, highlighting tirofiban's potential role in non-acute ischemic settings. While Yingdao

Chen and collaborators (2025) reported positive effects of tirofiban on neurological function and EEG parameters, they did not assess changes in inflammatory markers. A major strength of our study lies in its validation of tirofiban's dual benefit, which is suppressing both SCI and inflammation. Nevertheless, the lack of data on aneurysm size and comorbidities limits the generalizability of the results. Future research should include these variables to precisely identify the appropriate patient population most likely to benefit from tirofiban treatment.

Mechanistically, these beneficial effects of tirofiban are due to its dual action as a GPIIb/IIIa receptor inhibitor. By inhibiting platelet activation, tirofiban reduces the release of pro-inflammatory mediators such as P-selectin and Cluster of Differentiation 40 Ligand (CD40L), thereby blocking the interaction between platelets and neutrophils and suppressing neutrophils chemotaxis and infiltration to the site of vascular injury. Additionally, inhibition of platelet activation weakens the activation of monocytes/macrophages through the CD40-CD40L pathway, directly reducing the secretion of IL-6 and TNF-α. The decrease in IL-6 levels subsequently reduces hepatic synthesis of CRP, effectively interrupting the "peripheral inflammation-central injury" cascade (Caron et al, 2002; Zhuge et al, 2018; Marrone et al, 2024).

This anti-inflammatory effect of tirofiban may protect cognitive function through multiple mechanisms. First, pro-inflammatory factors such as IL-6 and TNF-α can either cross the damaged blood-brain barrier or be actively transported into the central nervous system, where they activate microglia and drive them toward a pro-inflammatory phenotype, releasing reactive oxygen species and nitric oxide, thereby directly damaging the neuronal synaptic structure in the hippocampus and prefrontal cortex (Luo et al, 2017). Second, TNF-α can upregulate the expression of complement protein C1q, promoting microglial phagocytosis of synapses, while increased IL-6 expression may inhibit the proliferation of neural stem cells, together leading to impaired synaptic plasticity and neurogenesis (Dion et al, 2023). Furthermore, platelet-mediated microthrombus formation may disrupt cerebral microcirculation, leading to localized ischemia that further exacerbates oxidative stress and mitochondrial dysfunction, whereas tirofiban can alleviate neuronal metabolic disorders by improving microcirculatory perfusion (Liu et al, 2024). Therefore, the anti-inflammatory effects of tirofiban not only reduce peripheral inflammatory markers but may also protect postoperative cognitive function by blocking the peripheral-central inflammatory axis. These observations suggest that antiplatelet drugs like tirofiban may exert a synergistic effect with "antithrombotic, anti-inflammatory, and neuroprotective" actions.

Furthermore, this study also found that tirofiban significantly reduced the incidence of asymptomatic cerebral infarction, possibly due to its potent antiplatelet effects. Antiplatelet drugs have been shown to reduce the incidence of asymptomatic cerebral infarction in patients with type 2 diabetic nephropathy (Kumar et al, 2014; Nakamura et al, 2005). Another study indicated that the occurrence of asymptomatic cerebral infarction is closely related to insufficient platelet inhibition, suggesting the potential need for more potent antiplatelet agents (Kim et al, 2012). The clinical significance of SCI, particularly its association with cog-

nitive dysfunction, should not be overlooked. Studies have shown that patients with asymptomatic cerebral infarction often experience varying degrees of cognitive decline, and in more severe cases, this can progress to dementia, significantly increasing the mortality rate (Zhao et al, 2012; Chaturvedi et al, 2023; Gupta et al, 2016). Cohort studies have shown that both symptomatic and asymptomatic cerebral infarctions have similar effects on cognitive decline, highlighting the need for recognizing and managing SCI in the clinical setting (Kühne et al, 2022; Raghavan et al, 2021; Vermeer et al, 2003). Asymptomatic cerebral infarction is closely related to overall cognitive decline and has been reported to more than double the risk of developing dementia (Vermeer et al, 2003). Therefore, reducing the incidence of asymptomatic cerebral infarction not only helps improve postoperative cognitive function but may also bring significant long-term benefits to patient prognosis.

In conclusion, this study suggests that the postoperative administration of tirofiban may improve cognitive dysfunction and reduce the incidence of SCI in patients with UIAs. The observed protective effects may be due to tirofiban's antiplatelet properties, its ability to reduce microthrombus formation, improve cerebral microcirculation, and exert anti-inflammatory actions. By combining antithrombotic, anti-inflammatory, and neuroprotective mechanisms, tirofiban offers comprehensive therapeutic benefits in managing UIAs.

However, several limitations of this study should also be acknowledged. First, the retrospective design of the study carries the risk of selection bias, limiting the strength of causal inferences. Second, cognitive function was assessed only within 72 hours postoperatively using the MoCA and MMSE scales. Although both tools are well-validated and frequently used in clinical settings, they primarily reflect overall cognitive status and do not capture domain-specific impairments in areas such as executive function, attention, and memory. Moreover, the study did not assess outcome indicators related to quality of life, such as those measured by the Assessment of Quality of Life (AQoL) scale. Meanwhile, the short-term follow-up may reflect only the acute phase of neuroprotection, without accounting for long-term cognitive recovery.

Future studies should extend the follow-up period to 3–6 months and incorporate comprehensive neuropsychological assessments such as the Trail Making Test and Stroop Test, along with functional outcome measures, to enable a more multidimensional and refined evaluation of cognitive impairment. Third, although a post hoc power analysis confirmed that sample size (n = 125) provided sufficient statistical power (0.99) to detect significant differences in MoCA scores, prospective studies should perform a priori sample size calculation to optimize the study design. Fourth, we did not record detailed aneurysm size or location beyond the dome-to-neck ratio used for inclusion, which limits our ability to assess the impact on outcomes. Similarly, other morphological data, such as wide-neck aneurysms, which may influence surgical complexity and postoperative inflammatory responses, were not collected. Given these limitations, prospective, randomized controlled trials are needed to further validate the cognitive benefits of tirofiban in UIA interventions. Such studies should also determine whether these effects are mediated through a reduction in SCI and explore associated changes in cognition-related biomarkers

and molecular signaling pathways, thereby providing more valuable guidance for clinical decision-making.

Conclusion

This study shows that tirofiban significantly improves cognitive function and reduces the incidence of asymptomatic cerebral infarction after endovascular embolization for UIAs. These protective effects are likely attributed to its antiplatelet activity, reduction in microthrombus formation, improvement in cerebral microcirculation, and antiinflammatory effects. Tirofiban may provide a comprehensive therapeutic benefit by combining "antithrombosis - antiinflammation - neuroprotection" mechanisms in managing UIAs. However, the observed improvement of approximately 1 point in cognitive scores has limited clinical relevance, warranting further study. Prospective trials are needed to validate these findings and assess the long-term cognitive and functional benefits of tirofiban.

Key Points

- Tirofiban significantly improves short-term cognitive function post-UIA embolization (MoCA, $p < 0.001$; MMSE, $p = 0.001$).
- Tirofiban reduces the incidence of silent cerebral infarction (OR = 0.34, $p = 0.029$), suggesting a neuroprotective potential.
- Antithrombotic and anti-inflammatory effects (reduction in CRP and IL-6, $p < 0.001$) likely underlie its benefits.
- The retrospective design, small sample size (n = 125), and short follow-up (72 hours) limit the assessment of long-term outcome.
- Missing aneurysm characteristics and comorbidity data are key limitations that require future investigation.
- Prospective randomized trials are needed to validate tirofiban's long-term cognitive benefits and applicability.

Availability of Data and Materials

The data and materials in the current study are available from the corresponding author on reasonable request.

Author Contributions

XB, PYH, XBL, WX and FFJ contributed to the design of the work. XB and DFY drafted the manuscript. FC, CXY, DFY, and FFJ contributed to the interpretation of the data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final version of the paper. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Affiliated Jinhua Hospital, Zhejiang University School of Medicine's Ethics Committee (Approval No. 2025490101) and was conducted following the principles outlined in the Declaration of Helsinki. Informed consent was obtained from the patients.

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Conflict of Interest

The authors declare no conflict of interest.

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