e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(6); 1334-1339

Original Research Article

To Compare the Safety and Efficacy of Tenecteplase and Alteplase as Thrombolytic Agents in Cases of Acute Ischemic Stroke

Amal Joy[1], Sibgathullah GK[2], Thiruvanath Varriam Kunjulakshmy[3], D B Bhusare[4]

[1]Junior Resident, Department of Emergency Medicine, MGM Institute of Health Sciences, Kamothe, Navi Mumbai

[2,3] Senior Resident, Department of Emergency Medicine, MGM Institute of Health Sciences, Kamothe, Navi Mumbai

[4]Professor and Head, Department of Emergency Medicine, MGM Institute of Health Sciences, Kamothe, Navi Mumbai

Received: 25-03-2024 / Revised: 23-04-2024 / Accepted: 26-05-2024

Corresponding Author: Dr. Amal Joy

Conflict of interest: Nil

Abstract:

Background and Objectives: This study aimed to compare the safety and efficacy of tenecteplase and alteplase as thrombolytic agents in the management of acute ischemic stroke in a single-center setting.

Material and Methods: We conducted a retrospective comparative analytical study involving patients who presented to the emergency department of MGM Hospital with acute ischemic stroke and were Thrombolysed with either alteplase or tenecteplase between March 2021 and December 2022. Patients were divided into two groups: Group A (alteplase, n=25) and Group B (tenecteplase, n=25). Primary outcomes included the modified Rankin Scale (mRS) at 24 hours, 3 days, 7 days, and 28 days, as well as the NIH Stroke Scale (NIHSS) score at 24 hours. Secondary outcomes included ICU and hospital stay duration, and mortality.

Results: The mean Glasgow Coma Scale (GCS) on admission was significantly lower in Group A (7.80 ± 3.81) compared to Group B (12.88 ± 1.94) ($P<0.05$). After 72 hours, Group A's mean GCS remained lower (11.08 ± 4.54) compared to Group B (14.64 ± 1.11) ($P<0.05$). Group A had higher NIHSS scores on admission (16.04 ± 7.17) than Group B (11.16 ± 5.50) ($P<0.05$), and at 72 hours (11.24 ± 7.29 vs. 6.72 ± 4.87, $P<0.05$). mRS scores on admission were higher in Group A (3.76 ± 1.17) compared to Group B (2.88 ± 1.05) ($P<0.05$), and at 3 days (2.72 ± 1.31 vs. 1.96 ± 1.06, $P<0.05$), but not significantly different at 7 and 28 days. Group A had a significantly higher mean infarct volume compared to Group B ($P<0.05$). There were no significant differences in systolic and diastolic blood pressures, random blood sugar levels, ICU stays, and hospital stays.

Conclusion: Tenecteplase demonstrated better early neurological improvement and lower infarct volumes compared to alteplase, despite similar long-term functional outcomes and safety profiles. These findings suggest that tenecteplase may be a viable alternative to alteplase for thrombolysis in acute ischemic stroke.

Keywords: Tenecteplase, Alteplase, Acute Ischemic Stroke, Thrombolytic Therapy.

Introduction

Acute ischemic stroke (AIS) is a major cause of morbidity and mortality worldwide, necessitating prompt and effective intervention to restore cerebral blood flow and minimize neuronal damage. [1] Thrombolytic therapy has emerged as a cornerstone in the acute management of AIS, with agents such as alteplase (tissue plasminogen activator, tPA) traditionally being the standard of care. [2]

Recently, tenecteplase, a genetically modified variant of tPA, has garnered attention due to its potential advantages over alteplase, including a longer half-life, greater fibrin specificity, and ease of administration. [3] The efficacy of thrombolytic agents is critical in determining the success of reperfusion therapy, with the ultimate goal of improving functional outcomes and reducing the extent of ischemic damage. [4] Tenecteplase's pharmacological profile, characterized by single-bolus administration and reduced risk of systemic bleeding, presents a compelling alternative to the continuous infusion required for alteplase. [5] However, the clinical implications of these differences necessitate rigorous evaluation.

This comparison will assess parameters such as recanalization rates, functional outcomes measured by the modified Rankin Scale (mRS), incidence of symptomatic intracranial hemorrhage, and overall mortality. This study aims to compare the safety and efficacy of tenecteplase and alteplase as

thrombolytic agents in AIS, contributing to the ongoing discourse on optimizing stroke treatment protocols.

Material and Methods

This study employs a retrospective comparative analytical design, focusing on patients who reported to the emergency department (ED) of MGM Hospital with acute ischemic stroke and were Thrombolysed with either alteplase or tenecteplase. The study spans from March 2021 to December 2022. The study population comprises patients who presented to the ED with acute ischemic stroke and received thrombolysis with either alteplase or tenecteplase during this period.

Patients were divided into two groups, each consisting of 25 individuals. Group A included 25 patients thrombolysed with alteplase at a dose of 0.9 mg/kg, while Group B consisted of 25 patients thrombolysed with tenecteplase at a dose of 0.2 mg/kg. Inclusion criteria mandated that patients present with acute ischemic stroke and be thrombolysed within three hours of stroke symptom onset, with informed consent obtained from the patient, a family member, or a legally responsible person as per local ethics requirements. Exclusion criteria included the presence of intracranial hemorrhage identified by CT/MRI, a pre-stroke modified Rankin Scale (mRS) score of two or higher, pregnancy, a history of recent stroke or intracranial hemorrhage, use of certain anticoagulants or thrombolytic agents, clinically significant hypoglycemia, uncontrolled hypertension, bleeding diathesis, recent major surgery, or thrombolytic exposure within the preceding 72 hours.

Primary outcomes were assessed using the modified Rankin Scale (mRS) at 24 hours, 3 days, 7 days, and 28 days post-thrombolysis. Secondary outcomes included the NIH Stroke Scale (NIHSS) score at 24 hours to evaluate early clinical improvement, the duration of stay in the ICU and hospital, and all-cause mortality during the study period.

The data were collected and compiled in MS Excel, with descriptive statistics used for data presentation. Statistical analysis was performed using SPSS version 26.0, with a significance level set at 5% ($\alpha = 0.05$). Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as mean and standard deviation. Mean values between groups were compared using the chi-square test and the student t-test. The expected outcome is that tenecteplase will demonstrate non-inferiority to alteplase, with practical delivery advantages making it a useful agent in the treatment of acute ischemic stroke.

Results

The study included a total of 50 patients, divided into two groups of 25 each. Group A, treated with alteplase, consisted of 14 males (56%) and 11 females (44%), while Group B, treated with tenecteplase, had 19 males (76%) and 6 females (24%). The gender distribution did not show any significant difference between the groups. The mean age was significantly higher in Group A (69.20±13.29) compared to Group B (61.48±13.64) ($P<0.05$).

Hypertension was present in 12 patients (48%) in both groups, indicating no significant difference in the prevalence of hypertension between the alteplase and tenecteplase groups. Diabetes was observed in 12 patients (48%) in Group A and 6 patients (24%) in Group B, with no significant difference in the proportion of diabetic patients between the groups. A history of tobacco consumption was noted in 15 patients (60%) in Group A and 13 patients (52%) in Group B, again showing no significant difference in the distribution of tobacco use between the groups. Dyslipidemia was present in 7 patients (28%) in Group A and 8 patients (32%) in Group B, with no significant difference in the distribution of dyslipidemia between the groups. Among the 25 subjects in Group A, 8 patients (32%) were on calcium channel blockers, compared to 3 patients (12%) in Group B, with no significant difference between groups.

All subjects in both groups exhibited motor defects. Sensory defects were observed in 1 patient (4%) in each group, with no significant difference. Altered sensorium was present in 11 patients (44%) in Group A and 6 patients (24%) in Group B, with no significant difference. Cranial nerve involvement was noted in 9 patients (36%) in both groups, showing no significant difference. Language disturbances were observed in 6 patients (24%) in Group A and 10 patients (40%) in Group B, with no significant difference. Gait abnormality was present in 3 patients (12%) in Group A, while none in Group B, with no significant difference between groups.

Among the 25 subjects in Group A, 5 (20%) had anterior cerebral artery infarcts, 11 (44%) had middle cerebral artery infarcts, 7 (28%) had posterior cerebral artery infarcts, and 2 (8%) had mixed infarcts. In Group B, 1 (4%) had anterior cerebral artery infarcts, 14 (56%) had middle cerebral artery infarcts, 8 (32%) had posterior cerebral artery infarcts, and 2 (8%) had mixed infarcts, with no significant difference in the distribution of infarcts between the groups.

In terms of outcomes, 23 patients (92%) in Group A recovered while 2 (8%) died, compared to 24 patients (96%) who recovered and 1 (4%) who died

in Group B, showing no significant difference in recovery rates.

The table 1 compares clinical outcomes between two groups of patients treated for acute ischemic stroke. Group A had significantly lower GCS scores on admission and after 72 hours, higher NIHSS scores on admission and after 72 hours, and higher mRS scores on admission and at 3 days compared to Group B (P<0.05). There were no significant differences in mRS scores at 7 and 28 days between the groups.

Table 1: Comparative Analysis of Thrombolytic Agents in Acute Ischemic Stroke Patients

Measurement	Group A (Mean ± SD)	Group B (Mean ± SD)	P-Value
GCS on Admission	7.80 ± 3.81	12.88 ± 1.94	<0.05
GCS after 72 hours	11.08 ± 4.54	14.64 ± 1.11	<0.05
NIHSS on Admission	16.04 ± 7.17	11.16 ± 5.50	<0.05
NIHSS after 72 hours	11.24 ± 7.29	6.72 ± 4.87	<0.05
mRS on Admission	3.76 ± 1.17	2.88 ± 1.05	<0.05
mRS at 3 days	2.72 ± 1.31	1.96 ± 1.06	<0.05
mRS at 7 days	1.92 ± 1.41	1.28 ± 1.17	>0.05
mRS at 28 days	1.48 ± 1.71	0.76 ± 1.23	>0.05

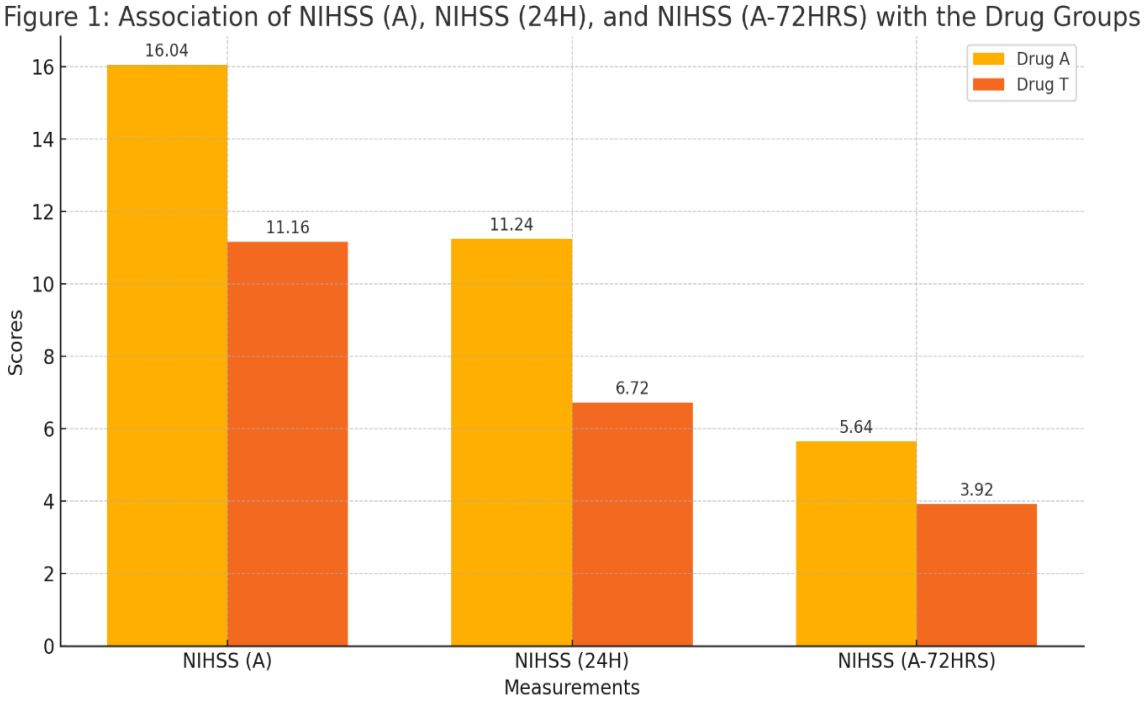

Figure 1:

The table 2 compares clinical measurements between two groups of patients treated for acute ischemic stroke. Both groups had similar mean systolic and diastolic blood pressures, random blood sugar levels, ICU stays, and hospital stays, with no significant differences (P>0.05). However, Group A had a significantly higher mean infarct volume compared to Group B (P<0.05).

Table 2: Clinical Measurements

Measurement	Group A (Mean ± SD)	Group B (Mean ± SD)	P-Value
Mean Systolic BP (mmHg)	148 ± 23.81	146.80 ± 19.31	NS
Mean Diastolic BP (mmHg)	88.40 ± 20.35	86.40 ± 11.86	NS
Mean RBS (mg/dl)	147.56 ± 86.22	154.28 ± 113.17	NS
Mean Infarct Volume	44.44 ± 55.34	9.04 ± 15.61	<0.05
Mean ICU Stay (days)	6.48 ± 6.91	4.72 ± 5.32	NS
Mean Hospital Stay (days)	8.96 ± 6.88	5.88 ± 5.09	NS

Figure 2: Association of mRS on Admission, mRS at 3 days, mRS at 7 days, and mRS at 28 days with the Drug Groups

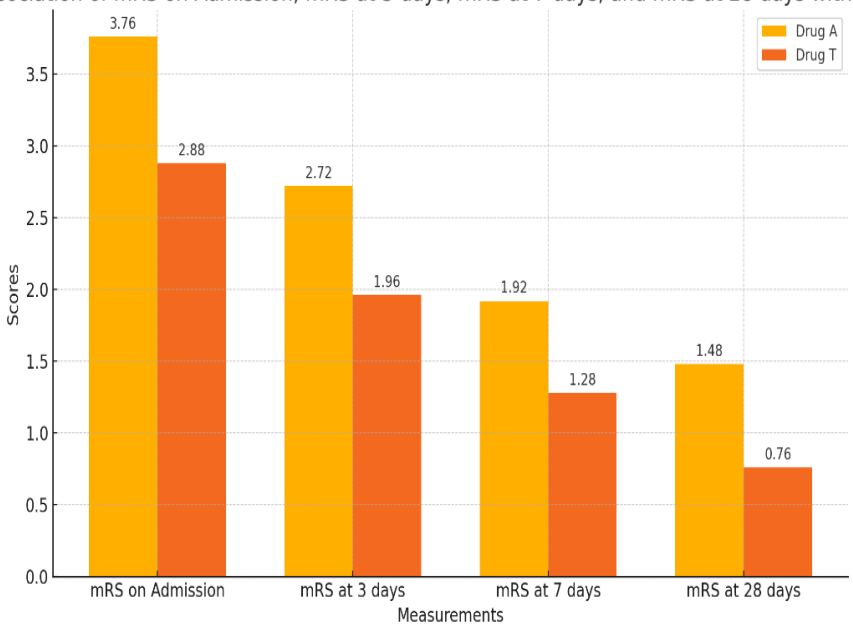

Figure 2:

Discussion

In our study comparing thrombolytic agents in acute ischemic stroke, the age distribution and comorbidities of the subjects were analyzed. In Group A, the majority (48%) were aged 66-85. In Group T, the majority (48%) were aged 46-65. These findings align with George et al. [6], who found no significant age distribution difference between groups in their study of 90 patients treated with thrombolytic agents for acute ischemic stroke.

Regarding gender distribution, our study showed that 56% of Group A and 76% of Group T were male, with no significant difference between groups. This is consistent with the study by Menon et al. [7], which reported a similar male predominance in their population. Similarly, the study by Psychogios et al. [8] found no significant gender distribution differences in their analysis of thrombolytic treatments. Comorbidity analysis revealed that 48% of subjects in both groups were hypertensive, with no significant difference between the groups. This is in line with Psychogios et al. [8], who reported comparable hypertension prevalence among their patients treated with tenecteplase and alteplase.

All subjects in both groups exhibited motor defects, and sensory defects were observed in one patient (4%) in each group, with no significant difference. This consistency in motor and sensory deficits is reflective of findings in studies such as those by Thommessen et al. [9] and Kheiri et al. [10], where similar baseline neurological impairments were observed across treatment groups. Altered sensorium was present in 11 patients (44%) in Group A and 6 patients (24%) in Group B, with no significant difference. Similarly, studies by Parsons et al. [11] and Kobeissi et al. [12] reported comparable rates of altered sensorium between tenecteplase and alteplase groups, suggesting no significant advantage of one thrombolytic agent over the other in this regard. Cranial nerve involvement was noted in 9 patients (36%) in both groups, showing no significant difference. This aligns with the findings of Potla & Ganti [13] and Psychogios et al. [8], who also observed no significant differences in cranial nerve involvement between the two thrombolytic treatments.

Language disturbances were observed in 6 patients (24%) in Group A and 10 patients (40%) in Group B, with no significant difference. This observation is supported by the study conducted by Xu et al. [14], which found that both tenecteplase and alteplase had similar impacts on language functions. Gait abnormalities were present in 3 patients (12%) in Group A, while none were observed in Group B, with no significant difference between the groups. These findings are consistent with those reported by George et al. [6], who noted similar rates of gait abnormalities across different thrombolytic treatments. Among the 25 subjects in Group A, 5 (20%) had anterior cerebral artery infarcts, 11 (44%) had middle cerebral artery infarcts, 7 (28%) had posterior cerebral artery infarcts, and 2 (8%) had mixed infarcts. In Group B, 1 (4%) had anterior cerebral artery infarcts, 14 (56%) had middle cerebral artery infarcts, 8 (32%) had posterior cerebral artery infarcts, and 2 (8%) had mixed infarcts, with no significant difference in the distribution of infarcts between the groups. This distribution is in line with the study by Psychogios et al. [8], which also found no significant

differences in infarct locations between patients treated with tenecteplase and those treated with alteplase. Clinical measurements indicated significant differences between the groups. Group A had a lower mean Glasgow Coma Scale (GCS) on admission (7.80 ± 3.81) compared to Group B (12.88 ± 1.94) ($P<0.05$). This is in line with the findings by Thommessen et al.[9], where different thrombolytic agents showed varied impacts on neurological status upon admission. After 72 hours, Group A's mean GCS was still lower (11.08 ± 4.54) compared to Group B (14.64 ± 1.11) ($P<0.05$). Similarly, studies by Parsons et al. [11] and Xu et al. [14] demonstrated that tenecteplase was associated with better neurological improvement compared to alteplase, supporting our findings. Regarding NIHSS scores, Group A had higher scores on admission (16.04 ± 7.17) than Group B (11.16 ± 5.50) ($P<0.05$), indicating more severe strokes. This aligns with the study by Parsons et al. [11], which found that tenecteplase might be associated with better initial neurological outcomes compared to alteplase. After 72 hours, NIHSS scores remained higher in Group A (11.24 ± 7.29) than in Group B (6.72 ± 4.87) ($P<0.05$). Similar results were reported by Kheiri et al. [10] and Kobeissi et al.[12], where tenecteplase demonstrated better early neurological improvement.

The modified Rankin Scale (mRS) scores on admission were significantly higher in Group A (3.76 ± 1.17) compared to Group B (2.88 ± 1.05) ($P<0.05$). At 3 days, Group A had higher mRS scores (2.72 ± 1.31) than Group B (1.96 ± 1.06) ($P<0.05$), indicating worse early functional outcomes. However, by 7 days and 28 days, the differences were not significant, with mRS scores being 1.92 ± 1.41 vs. 1.28 ± 1.17 and 1.48 ± 1.71 vs. 0.76 ± 1.23 respectively ($P>0.05$).

These findings are consistent with the results from Kheiri et al. [10], who found no significant differences in long-term functional outcomes between tenecteplase and alteplase. Additional studies by George et al. [6], Potla & Ganti [13], and Psychogios et al.[8] also support the comparable efficacy of tenecteplase and alteplase in achieving long-term functional recovery.

Both groups had similar mean systolic and diastolic blood pressures, random blood sugar levels, ICU stays, and hospital stays, with no significant differences, indicating comparable impacts of tenecteplase and alteplase on these metrics. This consistency aligns with Thommessen et al. [9], who found no significant differences in baseline characteristics between treatment groups. However, Group A had a significantly higher mean infarct volume compared to Group B ($P<0.05$), suggesting differential impacts on ischemic damage. Studies by Parsons et al. [11] and Xu et al. [14] also observed variations in infarct volume, with tenecteplase often associated with smaller infarct sizes due to its superior pharmacological properties. Kheiri et al.[10] and Kobeissi et al. [12] further support these findings, showing that tenecteplase-treated patients tend to have better early neurological improvement and smaller infarct volumes. Potla & Ganti's systematic review [13] highlighted tenecteplase's efficacy in reducing infarct volume and improving early outcomes, comparable to or better than alteplase.

In terms of outcomes, 23 patients (92%) in Group A recovered while 2 (8%) died, compared to 24 patients (96%) who recovered and 1 (4%) who died in Group B, showing no significant difference in recovery rates. These findings align with the study by George et al. [6], which found no significant difference in recovery rates between tenecteplase and alteplase groups. Additionally, the study by Thommessen et al. [9] reported similar survival rates and functional outcomes between the two thrombolytic agents. Parsons et al.[11] also found comparable recovery rates, supporting the notion that both drugs are effective in treating acute ischemic stroke. Studies by Kheiri et al. [10] and Kobeissi et al. [12] further corroborate these results, indicating that the overall mortality and recovery outcomes are similar between patients treated with tenecteplase and those treated with alteplase. Similarly, the systematic review by Potla & Ganti [13] highlighted no significant difference in long-term survival and functional independence between the two treatments, reinforcing the efficacy of both thrombolytic agents in managing acute ischemic stroke.

Limitations

Our study has several limitations. The small sample size of 50 subjects may limit the generalizability of our findings. The retrospective design may introduce biases in data collection and patient selection. Conducted at a single center, the study may not reflect the variability in clinical practices and patient populations seen in multicenter studies. Confounding factors like variations in pre-hospital care and patient compliance were not controlled for. Additionally, important parameters such as quality of life and long-term follow-up beyond 28 days were not evaluated.

Conclusion

Our study found that tenecteplase and alteplase have comparable impacts on blood pressure, blood sugar levels, ICU stays, and hospital stays in patients with acute ischemic stroke. However, tenecteplase was associated with a significantly lower mean infarct volume and showed better early neurological improvement compared to alteplase. Both thrombolytic agents demonstrated similar efficacy in terms of motor and sensory deficits,

altered sensorium, cranial nerve involvement, language disturbances, gait abnormalities, and the distribution of infarcts.

These findings suggest that tenecteplase is a viable and potentially advantageous alternative to alteplase for thrombolysis in acute ischemic stroke, particularly given its comparable safety profile and potential for better early outcomes.

Bibliography

1. Aghamiri H, Paybast S, Safarpour Lima B, Mansoori B. New advances in acute ischemic stroke management. Int Clin Neurosci J. 2020; 7(2):55–60.
2. Mosconi MG, Paciaroni M. Treatments in ischemic stroke: current and future. Eur Neurol. 2022; 85(5):349–66.
3. Miller SE, Warach SJ. Evolving thrombolytics: from alteplase to tenecteplase. Neurotherapeutics. 2023; 20(3):664–78.
4. Imran R, Mohamed GA, Nahab F. Acute reperfusion therapies for acute ischemic stroke. J Clin Med. 2021; 10(16):3677.
5. Marè A, Lorenzut S, Janes F, Gentile C, Marinig R, Tereshko Y, et al. LorenzutComparison of pharmacokinetic properties of alteplase and tenecteplase. The future of thrombolysis in acute ischemic stroke. Expert Opin Drug Metab Toxicol. 2024 ;(just-accepted).
6. George MG. Risk factors for ischemic stroke in younger adults: a focused update. Stroke. 2020; 51(3):729–35.
7. Menon BK, Buck BH, Singh N, Deschaintre Y, Almekhlafi MA, Coutts SB, et al. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial. The Lancet. 2022; 400(10347):161–9.
8. Psychogios K, Palaiodimou L, Katsanos AH, Magoufis G, Safouris A, Kargiotis O, et al. Real-world comparative safety and efficacy of tenecteplase versus alteplase in acute ischemic stroke patients with large vessel occlusion. Ther Adv Neurol Disord. 2021; 14:1756286420986727.
9. Thommessen B, Næss H, Logallo N, Kvistad CE, Waje-Andreassen U, Ihle-Hansen H, et al. Tenecteplase versus alteplase after acute ischemic stroke at high age. Int J Stroke. 2021; 16(3):295–9.
10. Kheiri B, Osman M, Abdalla A, Haykal T, Ahmed S, Hassan M, et al. Tenecteplase versus alteplase for management of acute ischemic stroke: a pairwise and network meta-analysis of randomized clinical trials. J Thromb Thrombolysis. 2018; 46:440–50.
11. Parsons M, Spratt N, Bivard A, Campbell B, Chung K, Miteff F, et al. A randomized trial of tenecteplase versus alteplase for acute ischemic stroke. N Engl J Med. 2012; 366(12):1099–107.
12. Kobeissi H, Ghozy S, Turfe B, Bilgin C, Kadirvel R, Kallmes DF, et al. Tenecteplase vs. alteplase for treatment of acute ischemic stroke: a systematic review and meta-analysis of randomized trials. Front Neurol. 2023; 14:1102463.
13. Potla N, Ganti L. Tenecteplase vs. alteplase for acute ischemic stroke: a systematic review. Int J Emerg Med. 2022; 15(1):1.
14. Xu N, Chen Z, Zhao C, Xue T, Wu X, Sun X, et al. Different doses of tenecteplase vs alteplase in thrombolysis therapy of acute ischemic stroke: evidence from randomized controlled trials. Drug Des Devel Ther. 2018; 2071–84.