Original Article

Barriers to Intravenous Alteplase within 4.5 Hours of Acute Ischemic Stroke Onset

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Background: Stroke is the leading cause of death and disability. Nowadays, the standard treatment is Intravenous thrombolytic with alteplase (t-PA) within 4.5 hours after the stroke onset. However, some patients who arrived to the hospital within 4.5 hours after stroke onset haven't received the alteplase.

Objective: To investigate the barriers to thrombolysis drug (alteplase) in acute ischemic stroke patients who arrived at the hospital within 4.5 hours after the stroke onset.

Materials and Methods: A retrospective study of ischemic stroke patients who developed stroke symptoms and arrived at the hospital within 4.5 hours but did not receive the thrombolytic drug (non-treatment group). Data were collected at the North-East hospital of Thailand from the hospital stroke registry and the patient record from October 2014 to September 2015. The study focused on the reasons for which this group of patients was excluded from receiving the thrombolytic drug. Factors associated with the non-treatment group were investigated using multivariable logistic regression.

Results: Of a total 229 patients who were diagnosed with acute ischemic stroke and arrived within 4.5 hours after stroke onset, 61 patients underwent thrombolytic therapy with alteplase. Of the 168 patients who did not receive the alteplase, the main reasons for this were mild or improving symptoms, contraindication to alteplase and uncertain onset time (including wake-up strokes). Factors associated with the non-treatment group were door time over three hours and patients who had an underlying history of hypertension or an old cerebrovascular accident (CVA). These patients were less likely to receive the thrombolytic drug. While patients with a National Institute of Health Stroke Scale (NIHSS) between 8 and 12, were more likely to receive the treatment.

Conclusion: Barriers to use of the thrombolytic drug in acute ischemic stroke in Thai patients included mild or improved symptoms, relative contraindication to alteplase and uncertain onset time. In order to increase alteplase administration, the revision of relative contraindication in mild symptoms, seizure at onset of stroke and wake-up stroke or stroke with an uncertain time of onset should be considered. The application of neuroimaging can be useful to select the eligible cases.

Keywords: Acute ischemic stroke, Thrombolytic therapy, Alteplase, t-PA, rt-PA, r-tPA

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Stroke is the leading cause of death and disability throughout the world. It happens when blood supply to the brain is compromised. Ischemic stroke is a common type of stroke that accounts for over 80 per cent of all acute strokes[1,2]. To date, the proven therapy for ischemic stroke is reperfusion therapies which allow blood flow to the ischemic brain to reduce disability and mortality[2,3]. Intravenous thrombolytic with alteplase (t-PA) is a treatment which shows a clear benefit for stroke onset within 4.5 hours[4]. However, a number of patients who arrived to the hospital within 4.5 hours after stroke onset did not received alteplase[2,5,6].

According to the previous studies, the percent of ischemic stroke patients who received alteplase treatment varied. In the United States, the alteplase administration rate was reported at around 2 to 5 percent from all acute ischemic stroke patients[6]. Some literature presented a high rate of over 20 percent[7,8]. Srinagarind Hospital is a stroke centre. It admits ischemic stroke patients who are referred from a nearby hospital in the North-East of Thailand. The administration of alteplase in Srinagarind hospital accounts for a high rate of administration compared to a national study[9], however, the rate of alteplase declined from 13.48 percent in 2014 to 10.67 percent in 2015. This study aims to investigate barriers to thrombolytic therapy by examining characteristics of ischemic stroke patients who had stroke onset within 4.5 hours but did not receive reperfusion therapy with alteplase.

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Materials and Methods

Design and setting

A retrospective study of ischemic stroke patients who were admitted to the stroke unit at Srinagarind Hospital in Thailand, from October 2014 to September 2015 was used. All patients who developed stroke symptom onset within 4.5 hours were enrolled in stroke fast track care. Through this system, patients receive care from a multidisciplinary team to ensure that they reach the target time for thrombolytic treatment. The study targets a group of ischemic stroke patients aged over 18 who arrived at the hospital within 4.5 hours but did not receive alteplase. Data were collected from the hospital stroke registry and the patient record. The study was approved by the Khon Kaen University Ethics Committee in Human Research (HE591190).

Statistical analysis

The proportion of ischemic stroke patients who did not receive alteplase and their characteristics were calculated using percentage. Chi-square test or Fisher's exact test was calculated for the difference between groups of patients who received and did not receive alteplase. A *p*-value lower than 0.05 was considered as statistically significant. Factors associated with the non-treatment group were investigated using univariable and multivariable logistic regression for crude and adjusted odds ratio and 95% confidence intervals. All analyses were done using STATA version 10.

Results

Overall, of the 302 patients who developed stroke symptoms within the onset of 4.5 hours, 229 patients were diagnosed with acute ischemic stroke (Figure 1). Sixty-one patients underwent thrombolysis therapy with alteplase, while 168 patients did not receive alteplase. Baseline characteristics are presented in Table 1. The mean age of the studying group (non-treatment with alteplase group) was 65.38. The majority of non-treatment patients walked into the hospital, and only 37 percent of them were brought in by emergency medical services or transferred from other hospitals. The mean of the door to CT time in the non-treatment group was 26.85. Patients in the non-treatment group carried a higher burden of comorbidity such as diabetes, hypertension, dyslipidemia and old cerebrovascular disease. NIHSS and Glasgow Coma Scores that were first assessed at the emergency department showed that the treatment group had a higher severity of disease at presentation.

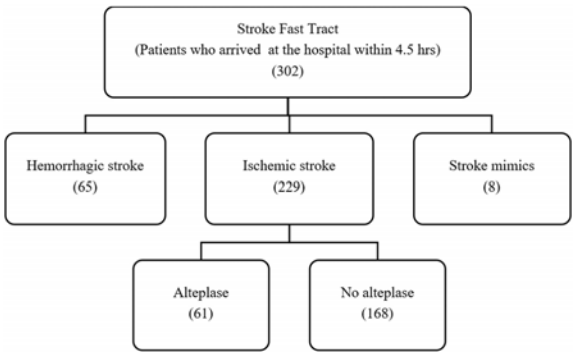

Figure 1. Study flow of the patients who enrolled in stroke fast tract care, and received and did not receive intravenous alteplase.

Of 168 ischemic stroke patients who arrived at the hospital within 4.5 hours, over 80 per cent of them reached the hospital within 3 hours of the onset of symptoms. The main reasons for not including them in alteplase therapy (Table 2) were that 95 patients had mild symptoms of stroke or improved, 31 of them had contraindication for thrombolysis therapy and 28 of them presented with onset within 4.5 hours however, they had uncertain onset time, or it was a wake-up stroke. Eleven patients denied the treatment; two patients had an end-stage disease, and in four patients, the hospital process could not reach the target time of 4.5 hours.

The calculation for the association between characteristics of ischemic stroke patients and the exclusion from rt-PA treatment is presented in Table 3, using univariate and multivariate analysis. For univariate analysis, NIHSS over 8, GCS of 8 to 12, ischemic stroke patients who had an underlying history of hypertension and old CVA were associated with the non-treatment group. However, the multivariate showed that onset to door time over three hours and patients who had an underlying of hypertension or old CVA had a lower chance of receiving rT-PA, while NIHSS between 8 and 12 had a higher possibility of receiving alteplase therapy.

Discussion

This present study has confirmed the previous finding by Barber[8], Garcia-Monco[10] and Patcharaporn[11] that for most acute ischemic stroke patients who arrived at the hospital in time for the rt-PA therapy but did not receive therapy, this was because their symptoms were mild or improving. While Reiff[12] and Cocho[13] found that in-hospital processes, such as admission delay and neurological consultation delays were the primary reasons that patients did not receive alteplase. This reason contrasted with the present study, in which the delay in hospital process accounted for less than three per cent of patients who did not receive the treatment.

The NIHSS score relates to the volume of stroke lesion. NIHSS scores over 25 are considered as a contraindication for rt-PA administration. However, mild scores of NIHSS patients are treated differently from hospital to hospital as the benefits of thrombolysis in this group are not clear. Some hospitals defined mild symptoms as an NIHSS score less than 5[14]. The mild symptom patients in the present study include patients with an NHISS score of less than 4 and did not have aphasia or hemianopia symptoms. These criteria follow the American Stroke Association. Previous studies showed that 25 to 28 percent of patients

Table 1. Characteristics of acute ischemic stroke patients who received alteplase and those who were excluded from alteplase (non-treatment group)

	Alteplase treatment group (n = 168)	Non-treatment group (n = 61)	*p*-value
Male, n (%)	89 (52.98)	24 (39.34)	0.07
Age, mean ± SD	63.38±14.86	63.88±14.61	0.50
Mode of arrival, n (%)			0.08
Walk-in	105 (62.5)	28 (45.90)	
EMS	15 (8.93)	8 (13.11)	
Transfer	58 (28.57)	25 (40.98)	
Onset to door time <180 min, n (%)	139 (82.74)	55 (90.16)	0.167
Door to CT time (min), mean ± SD	26.85±34.95	18.55±15.42	0.06
Door to thrombosis (min), mean ± SD	120.28±71.65		
NIHSS score at admission, n (%)			<0.001
0 to 7	133 (79.17)	21 (34.43)	
8 to 14	19 (11.31)	19 (31.15)	
15 to 42	16 (9.52)	21 (34.43)	
GCS at admission, n (%)			0.03
8 to 12	149 (91.41)	47 (81.03)	
13 to 15	14 (8.59)	11 (18.97)	
Comorbidities, n (%)			
Diabetes	57 (33.93)	13 (21.31)	0.07
Hypertension	106 (63.10)	27 (44.26)	0.01
Dyslipidaemia	56 (33.33)	17 (27.87)	0.43
Arrhythmia	29 (17.26)	13 (21.31)	0.49
Old CVA	51 (30.36)	5 (8.20)	0.00
Cancer	10 (5.95)	3 (4.92)	0.71

Table 2. The reasons for exclusion of 168 patients from alteplase

Factors	Number of patients	Percentage
Uncertainty of onset time or wake-up stroke	24	14.28
Delay in hospital process	4	2.38
Absolute contraindications to alteplase		
History of intracranial hemorrhage	4	2.38
Coagulopathy (anticoagulant therapy)	4	2.38
Active internal bleeding (gastrointestinal bleeding)	1	0.59
Cerebrovascular accident within three months	10	5.95
Relative contraindications to alteplase		
Large area of infarction	6	3.57
Seizure at onset	4	2.38
Myocardial infarction within three months	1	0.59
External bleeding	1	0.59
Severity of disease		
NIHSS score <4	59	35.12
Improving symptoms	36	21.43
NIHSS score >18	1	0.59
Other reasons		
Patients or family members refused consent	11	6.54
Delay in hospital process	4	2.38
Terminal stage patients	2	1.18

who present with mild signs of stroke could deteriorate to a more severe disability or death[14,15]. Nevertheless, the randomized controlled trial study of administering rt-PA in mild symptom ischemic stroke patients did not show a significant benefit but increased the risk of bleeding[16]. In the present study, there were only 59 patients who presented with mild symptoms, and results showed the improvement of the total NIHSS score before discharge from the hospital in the non-treatment group. However, the patients who scored less than eight were also significantly excluded to the

Table 3. The association between the characteristics of ischemic stroke patients and the non-treatment with alteplase group

Patient characteristics	Univariate			Multivariate		
	OR	*p*-value	95% CI	OR	*p*-value	95% CI
Male	1.74	0.07	0.97 to 3.15			
Mode of arrival						
Walk-in	2	0.15	0.77 to 5.19			
EMS	Ref				Ref	
Transfer	1.024	0.96	0.38 to 2.74			
Onset to door time >180 min	1.91	0.17	0.75 to 4.86	4.32	0.01	1.36 to 13.64
NIHSS score at admission						
0 to 7	Ref					
8 to 14	0.16	<0.001	0.07 to 0.35	0.31	0.03	0.18 to 0.86
15 to 42	0.12	<0.001	0.05 to 0.26	0.71	0.54	0.24 to 2.12
GCS at admission, %						
8 to 12	0.4	0.036	0.17 to 0.94	2.27	0.248	0.56 to 9.15
13 to 15	Ref				Ref	
Comorbidities						
Diabetes	1.89	0.07	0.95 to 3.78			
Hypertension	2.15	0.01	1.18 to 3.90	4.05	0.001	1.77 to 9.25
Dyslipidaemia	1.29	0.43	0.68 to 2.46			
Arrhythmia	0.77	0.49	0.37 to 1.60			
Old CVA	4.88	0.001	1.85 to 12.90	8.97	<0.001	2.72 to 29.61
Cancer	1.22	0.77	0.32 to 4.60			

non-treatment group (from univariate and multivariate analysis). A similar finding was reported in Spain, where patients with an NIHSS score less than eight had a lower rate of alteplase than other groups[10]. However, we limited this to subgroup analysis between the group of the NIHSS less than four and the NIHSS of four to seven. The significance of the NHISS score zero to seven group may result from the patients with an NIHSS score of less than four. The further subgroup analysis and the focus on the outcome of NIHSS scores between 4 and 7 should be followed-up.

The second reason that prevented patients from alteplase was that they had a contraindication to rt-PA. Nineteen of thirty-one were excluded because they had absolute contraindication and 12 patients had a relative contraindication to rt-PA. Six patients did not received rt-PA because of a large ischemic area. The large area of infarction size can increase the risk of bleeding from rt-PA therapy. The study of early ischemic changes (EICs) on CT, showed that patients have a higher risk of bleeding when received rt-PA in the ischemic lesion involving over one-third of the middle cerebral artery territory, but this had no statistical significance[17]. For current practice, even though large areas of infarction are not included in absolute contraindication, the present large area of clear hypoattenuation is not recommended for rt-PA therapy[18].

Four patients who had a seizure at the onset were excluded from alteplase. This is because their symptoms could result from postictal Todd's paralysis[19,20]. Previous studies argued that the risk of bleeding in this group is very low[21-23]. There is also not enough evidence of negative outcomes in the use of alteplase in this group of patients[24]. The American Heart Association and American Stroke Association proposed that alteplase is reasonable for patients who have a seizure at onset of stroke[18]. However, seizure at the onset is still classified in a relative contraindication.

The third reason for not receiving alteplase therapy is because of a wake-up stroke or uncertain onset time. Despite providing an onset within 4.5 hours, some patients and their family cannot give an exact time of onset. Wake-up stroke patients are mostly excluded from eligibility since it is difficult to know the precise onset time[25]. The evidence from neuroimaging is now used to evaluate the management of wake-up stroke or stroke with unknown onset time[26-28]. A study assumed that wake-up stroke may occur just before time of wake up because there are not differences between the CT images of wake-up stroke patients and patients who knew an exact onset time of less than three hours[29]. A study using magnetic resonance imaging (MRI) can differentiate early strokes from strokes with an onset of over three or six hours[18,25]. Though using the diffusion weight imaging from MRI, patients who present with fluid-attenuated inversion recovery are more likely to have an early stroke which can be a candidate for alteplase[25,26].

Conclusion

Barriers to the thrombolytic drug in acute ischemic stroke in Thai patients were if they had mild or improved symptoms, relative contraindication to alteplase and uncertain onset times. In order to increase the rate of intravenous alteplase, the revision of the role of alteplase in those with

mild symptoms, seizure at the onset of stroke and wake-up stroke or stroke with an uncertain time of onset should be considered. The use of neuroimaging or a tissue clock can be helpful to select an eligible case for alteplase.

What is already known in this topic?

The alteplase given within 4.5 hour of the onset of acute stroke are widely used as the standard treatment. However, in practice, some patients have not received this treatment because of some reasons such as the patients have contraindication of alteplase and other reasons that were not known at the time.

What this study adds?

This study demonstrated that mild symptom of acute stroke or improved symptoms, relative contraindication to alteplase and uncertain onset times were the barriers of thrombolytic drug in acute ischemic stroke in Thai patients. Some special situation such as wake up stroke should be considered for given alteplace by using special imaging.

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Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Carrera E, Maeder-Ingvar M, Rossetti AO, Devuyst G, Bogousslavsky J. Trends in risk factors, patterns and causes in hospitalized strokes over 25 years: The Lausanne Stroke Registry. Cerebrovasc Dis 2007;24: 97-103.
2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics-2016 update: A report from the American Heart Association. Circulation 2016;133:e38-360.
3. Prasad K, Kaul S, Padma MV, Gorthi SP, Khurana D, Bakshi A. Stroke management. Ann Indian Acad Neurol 2011;14(Suppl 1):S82-96.
4. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581-7.
5. O'Connor RE, McGraw P, Edelsohn L. Thrombolytic therapy for acute ischemic stroke: why the majority of patients remain ineligible for treatment. Ann Emerg Med 1999;33:9-14.
6. Miller DJ, Simpson JR, Silver B. Safety of thrombolysis in acute ischemic stroke: a review of complications, risk factors, and newer technologies. Neurohospitalist 2011;1:138-47.
7. Quain DA, Parsons MW, Loudfoot AR, Spratt NJ, Evans MK, Russell ML, et al. Improving access to acute stroke therapies: a controlled trial of organised pre-hospital and emergency care. Med J Aust 2008;189:429-33.
8. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. Neurology 2001;56:1015-20.
9. Tanpradit E, Vorasoot N, Kasemsap N, Tiamkao S, Sawanyawisuth K, Kongbunkiat K. The rt-PA treatment in acute ischemic stroke: a national database study. J Med Assoc Thai 2020;103:77-80.
10. Garcia-Monco JC, Pinedo A, Escalza I, Ferreira E, Foncea N, Gomez-Beldarrain M, et al. Analysis of the reasons for exclusion from tPA therapy after early arrival in acute stroke patients. Clin Neurol Neurosurg 2007;109:50-3.
11. Somhanwong P, Binhosen V, Pakdevong N. Situation of care management in persons with stroke at Emergency Department, Bumrungrad International Hospital. J Nurs Health Care 2012:30;73-81.
12. Reiff T, Michel P. Reasons and evolution of non-thrombolysis in acute ischaemic stroke. Emerg Med J 2017;34:219-26.
13. Cocho D, Belvis R, Marti-Fabregas J, Molina-Porcel L, Diaz-Manera J, Aleu A, et al. Reasons for exclusion from thrombolytic therapy following acute ischemic stroke. Neurology 2005;64:719-20.
14. Smith EE, Fonarow GC, Reeves MJ, Cox M, Olson DM, Hernandez AF, et al. Outcomes in mild or rapidly improving stroke not treated with intravenous recombinant tissue-type plasminogen activator: findings from get with the guidelines-stroke. Stroke 2011;42: 3110-5.
15. Nedeltchev K, Schwegler B, Haefeli T, Brekenfeld C, Gralla J, Fischer U, et al. Outcome of stroke with mild or rapidly improving symptoms. Stroke 2007;38:2531-5.
16. National Institute of Neurological Disorders Stroke rt-PA Stroke Study Group. Recombinant tissue plasminogen activator for minor strokes: the National Institute of Neurological Disorders and Stroke rt-PA Stroke Study experience. Ann Emerg Med 2005;46:243-52.
17. Larrue V, von Kummer RR, Muller A, Bluhmki E. Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European-Australasian Acute Stroke Study (ECASS II). Stroke 2001;32:438-41.
18. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, et al. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: A statement for healthcare professionals from the American Heart Association/American Stroke

Association. Stroke 2016;47:581-641.
19. Selim M, Kumar S, Fink J, Schlaug G, Caplan LR, Linfante I. Seizure at stroke onset: should it be an absolute contraindication to thrombolysis? Cerebrovasc Dis 2002;14:54-7.
20. Fugate JE, Rabinstein AA. Absolute and relative contraindications to IV rt-PA for acute ischemic stroke. Neurohospitalist 2015;5:110-21.
21. Chernyshev OY, Martin-Schild S, Albright KC, Barreto A, Misra V, Acosta I, et al. Safety of tPA in stroke mimics and neuroimaging-negative cerebral ischemia. Neurology 2010;74:1340-5.
22. Zinkstok SM, Engelter ST, Gensicke H, Lyrer PA, Ringleb PA, Artto V, et al. Safety of thrombolysis in stroke mimics: results from a multicenter cohort study. Stroke 2013;44:1080-4.
23. Winkler DT, Fluri F, Fuhr P, Wetzel SG, Lyrer PA, Ruegg S, et al. Thrombolysis in stroke mimics: frequency, clinical characteristics, and outcome. Stroke 2009;40:1522-5.
24. Polymeris AA, Curtze S, Erdur H, Hametner C, Heldner MR, Groot AE, et al. Intravenous thrombolysis for suspected ischemic stroke with seizure at onset. Ann Neurol 2019;86:770-9.
25. Rubin MN, Barrett KM. What to do with wake-up stroke. Neurohospitalist 2015;5:161-72.
26. Huang X, Alakbarzade V, Khandanpour N, Pereira AC. Management of a wake-up stroke. Pract Neurol 2019;19: 326-31.
27. Hirano T. Searching for salvageable brain: the detection of ischemic penumbra using various imaging modalities? J Stroke Cerebrovasc Dis 2014;23:795-8.
28. Albers GW. Expanding the window for thrombolytic therapy in acute stroke. The potential role of acute MRI for patient selection. Stroke 1999;30:2230-7.
29. Huisa BN, Raman R, Ernstrom K, Tafreshi G, Stemer A, Meyer BC, et al. Alberta stroke program early CT Score (ASPECTS) in patients with wake-up stroke. J Stroke Cerebrovasc Dis 2010;19:475-9.

อุปสรรคในการให้ยา alteplase ทางหลอดเลือดดำในผู้ป่วยสมองขาดเลือดเฉียบพลันใน 4.5 ชั่วโมง

สุขสันต์ คำนวณศิลป์, มธุรส บูรณศักดา, ดนุ เกษรศิริ, กมลวรรณ เอี้ยงฮง, กรกฎ อภิรัตน์วรากุล, สมศักดิ์ เทียมเก่า

ภูมิหลัง: โรคหลอดเลือดสมองเป็นสาเหตุความพิการและการตายที่สำคัญ ปัจจุบันการรักษาภายใน 4.5 ชั่วโมงแรกของอาการคือการให้ยา alteplase ทางหลอดเลือดดำ อย่างไรก็ตามมีผู้ป่วยส่วนหนึ่งที่ไม่ได้ยาดังกล่าว

วัตถุประสงค์: เพื่อหาสาเหตุและอุปสรรคในการให้ยา alteplase ในผู้ป่วยโรคหลอดเลือดสมองที่มีอาการภายใน 4.5 ชั่วโมง

วัสดุและวิธีการ: การศึกษาย้อนหลังในผู้ป่วยโรคหลอดเลือดสมองที่มีอาการภายใน 4.5 ชั่วโมงแต่ไม่ได้รับยา alteplase โดยข้อมูลเก็บจากโรงพยาบาลในภาคตะวันออกเฉียงเหนือของประเทศไทยระหว่างเดือนตุลาคม พ.ศ. 2557 ถึง เดือนกันยายน พ.ศ. 2558 โดยมุ่งศึกษาหาสาเหตุในกลุ่มที่ไม่ได้รับยา alteplase และนำข้อมูลมาวิเคราะห์หาความสัมพันธ์

ผลการศึกษา: ผู้ป่วยทั้งหมด 229 ราย ที่ได้รับการวินิจฉัยว่าเป็นโรคสมองขาดเลือดและมาโรงพยาบาลภายใน 4.5 ชั่วโมงหลังเริ่มมีอาการได้รับยา 61 ราย ไม่ได้รับยา 168 ราย เหตุผลหลักของการไม่ได้รับยาคือ มีอาการเล็กน้อยหรืออาการดีขึ้น, มีข้อห้ามในการให้ยา, ไม่แน่ใจเรื่องเวลาที่เริ่มมีอาการ ในผู้ป่วยที่ได้รับยามีค่าคะแนน NIHSS 8 ถึง 12 คะแนน

สรุป: อุปสรรคในการให้ยา alteplase ในผู้ป่วยโรคสมองขาดเลือดคือ มีอาการเล็กน้อยหรืออาการดีขึ้น, มีข้อห้ามในการให้ยาและไม่แน่ใจเรื่องเวลาที่เริ่มมีอาการ