Original Article

The rt-PA Treatment in Acute Ischemic Stroke: A National Database Study

Tanpradit E, MD[1,2], Vorasoot N, MD[1,3], Kasemsap N, MD[1,3], Tiamkao S, MD[1], Sawanyawisuth K, MD, PhD[1,2], Kongbunkiat K, MD[1,3]

[1] Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[2] Sleep Apnea Research Group, Research Center in Back, Neck and Other Joint Pain and Human Performance, Research and Training Center for Enhancing Quality of Life of Working Age People, Khon Kaen University, Khon Kaen, Thailand
[3] North-Eastern Stroke Research Group, Khon Kaen University, Khon Kaen, Thailand

Objective: To evaluate the treatment outcomes of an intravenous recombinant tissue plasminogen activator (rt-PA) therapy in acute ischemic stroke from a national database.

Materials and Methods: The present study was a retrospective analytical study. The database used in the present study was a Universal Health Coverage (UHC) insurance of Thailand. The inclusion criteria were consecutive adult patients diagnosed as acute ischemic stroke and admitted to the hospital. The study period was between October 1st, 2004 to January 31st, 2013. The authors compared stroke outcomes, and stroke complications between those who received and did not receive the rt-PA treatment.

Results: During the study period, there were 244,032 patients met the study criteria. Of those, 2,102 patients (0.9%) received the rt-PA treatment. The rt-PA group had significant better discharge statuses than the no rt-PA group except death (6.9% vs. 6.0%; *p*-value = 0.151). There were six significant differences in terms of stroke complications between both groups. The rt-PA group had higher rates of complication in five items than the no rt-PA group. The no rt-PA group had only significant higher rate of sepsis than the rt-PA group (3.4% vs. 2.8%; *p*-value = 0.015).

Conclusion: The rt-PA treatment in acute ischemic stroke patients with the UHC had benefit on discharge status. Some complications of stroke in the rt-PA treatment were significantly higher than no rt-PA treatment.

Keywords: Functional status, Outcomes, Complications

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Stroke is a common neurological condition that may lead to morbidity and mortality. An intravenous recombinant tissue plasminogen activator (rt-PA) therapy within 4.5 hours of stroke onset is recommended[(1)]. The rt-PA improves physical function evidenced by several randomized trials. A meta-analysis published in 2014 showed that the rt-PA may be given after stroke onset of six hours[(2)]. However, symptomatic intracranial hemorrhage and deaths may be increasing.

Several studies conducted in Thailand showed the benefits of the rt-PA treatment[(3-6)]. These studies conducted in community hospitals or university hospitals with more severe strokes and showed beneficial effects of the rt-PA treatment. For example, the rt-PA treatment had better favorable outcomes significantly in large middle cerebral artery infarction (39% vs. 17%; *p*-value <0.001) than those who did not receive the rt-PA treatment. However, these studies conducted in few hospitals in Thailand. Therefore, this study aimed to evaluate the treatment outcomes of the rt-PA therapy in a national database.

Correspondence to:
Kongbunkiat K.
Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-43-363654, **Fax:** +66-43-347542
E-mail: kannikarkon@kku.ac.th

Materials and Methods

The present study was a retrospective analytical study. The database used in this study was a Universal Health Coverage (UHC) insurance of Thailand which covers approximately over 90% of Thai population. The inclusion criteria were consecutive adult patients diagnosed as acute ischemic stroke and admitted to the hospital. The study period was between October 1st, 2004 to January 31st, 2013. We searched the database by using the ICD 10 code I60 to I63.

All eligible patients were categorized as received the rt-PA treatment or not. The studied variables included baseline characteristics, regions of hospitals, co-morbid diseases, stroke severity, stroke outcomes, and stroke/rt-PA complications. The stroke severity was assessed by evidence of intubation, craniotomy/craniectomy, and tracheostomy

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procedures. For stroke outcomes, the main evaluation was based on discharge status which was categorized as death, improved, complete recovery, and not improved. These statuses were summarized by the attending physician on the discharge form.

Statistical analyses

Descriptive statistics were used to calculate mean (SD) and proportions in numerical and categorical variables, respectively. Differences between factors between two groups were executed by the Fisher-Exact test. The statistical analyses were computed by the STATA software, version 10.1 (College Station, Texas, USA).

Results

During the study period, there were 244,032 patients met the study criteria. Of those, 2,102 patients (0.9%) received the rt-PA treatment. The average age (SD) of all patients was 65.2 (13.8) years and male sex accounted for 52.7% as shown in Table 1. The patients from the eastern area of Thailand received the rt-PA treatment at the highest rate (27.2%). The most common co-morbid disease was hypertension (45.2%).

Regarding outcomes, the rt-PA group had longer length of stay than the no rt-PA group (7.8 vs. 5.8 days). For the stroke severity outcomes, the rt-PA group had significant higher proportions than the no rt-PA group in all three factors including intubation, craniotomy/craniectomy, and tracheostomy (Table 2). The rt-PA group had significant better discharge statuses than the no rt-PA group except death (6.9% vs. 6.0%; *p*-value = 0.151). There were six significant differences in terms of stroke/rt-PA complications between both groups. The rt-PA group had higher rates of complication in five items than the no rt-PA group. The no rt-PA group had only significant higher rate of sepsis than the rt-PA group (3.4% vs. 2.8%; *p*-value = 0.015).

Table 1. Characteristics of acute ischemic stroke patients who registered in the universal coverage database from October 1, 2011 to September 30, 2014 categorized by recombinant tissue plasminogen activator therapy (rt-PA)

Factors	No rt-PA (n = 241,930)	Rt-PA (n = 2,102)	Total (%) (n = 244,032)
Mean (SD) age, years	65.2 (13.8)	62.9 (13.0)	65.2 (13.8)
Age range, years			
<20	1,206 (0.5)	10 (0.5)	1,216 (0.5)
20 to 29	1,634 (0.7)	13 (0.6)	1,647 (0.7)
30 to 39	6,290 (2.6)	69 (3.3)	6,359 (2.6)
40 to 49	22,689 (9.4)	228 (10.9)	22,917 (9.4)
50 to 59	44,903 (18.6)	450 (21.4)	45,353 (18.6)
60 to 69	63,483 (26.2)	619 (29.5)	64,102 (26.3)
70 to 79	67,744 (28.0)	546 (26.0)	68,290 (28.0)
>80	33,981 (14.1)	167 (7.9)	34,148 (14.0)
Male sex	127,392 (52.7)	1,147 (54.6)	128,539 (52.7)
Regions			
Bangkok	39,889 (16.5)	399 (19.0)	40,288 (16.5)
North	59,169 (24.5)	416 (19.8)	59,585 (24.4)
Central	23,793 (9.8)	301 (14.3)	24,094 (9.9)
East	65,945 (27.3)	510 (24.3)	66,455 (27.2)
Northeast	31,192 (12.9)	231 (11.0)	31,423 (12.9)
South	21,940 (9.1)	245 (11.7)	22,185 (9.1)
Comorbid diseases			
Coronary artery disease	10,644 (4.4)	122 (5.8)	10,766 (4.4)
Hypertension	109,237 (45.2)	999 (47.5)	110,236 (45.2)
Diabetes	50,576 (20.9)	386 (18.4)	50,962 (20.9)
Obesity	293 (0.1)	9 (0.4)	302 (0.1)
Hyperthyroidism	1,985 (0.8)	36 (1.7)	2,021 (0.8)
Dyslipidemia	69,819 (28.9)	749 (35.6)	70,568 (28.9)
Heart failure	4,730 (2.0)	78 (3.7)	4,808 (2.0)
Rheumatic heart disease	4,037 (1.7)	84 (4.0)	4,121 (1.7)
Atrial fibrillation	20,577 (8.5)	459 (21.8)	21,036 (8.6)
Chronic kidney disease	8,702 (3.6)	65 (3.1)	8,767 (3.6)
Previous stroke	376 (0.2)	6 (0.3)	382 (0.2)
Previous transient ischemic attack	546 (0.2)	15 (0.7)	561 (0.2)
HIV infection	1,179 (0.5)	5 (0.2)	1,184 (0.5)
Peripheral artery disease	301 (0.1)	4 (0.2)	305 (0.1)

Discussion

The UHC national database showed that the rt-PA treatment rate in acute ischemic stroke was 0.9%. This rate was quite low compared with the US at 8% in the US even in the year of 2005[7]. However, low rate of the rt-PA use in Thailand may be from several reasons including healthcare system (travel time, location, training skills, facilities), or system-focused intervention[8].

As previously reported, the rt-PA treatment in the UHC insurance scheme also showed benefits of the rt-PA treatment compared with no rt-PA treatment including better discharge status (Table 2). However, this study was unable to show better mortality benefit of the rt-PA treatment. The US real world study found that the rt-PA reduced mortality by 48% (Adjusted hazard ratio of 0.52; 95% CI of 0.30 to 0.90)[9]. These findings may be due to more severe cases of the rt-PA group in this study (Table 2). The rt-PA group had more proportions of patients with intubation, craniectomy, or tracheostomy than the no rt-PA group significantly.

Even though the rt-PA treatment had favorable outcomes particularly on functional status, there were some complications of it. The rate of intracerebral hemorrhage from the rt-PA treatment in the present study was comparable with a previous study from Thailand (approximately 6%)[3]. Systemic bleeding, gastrointestinal bleeding in this study, is another complication from the rt-PA treatment that should be aware. For other stroke complications in this study may need further investigations to explain these findings.

The advantage of the present study is large study sample size which may represent the country. However, there are some limitations. First, the data were extracted from the summary discharge. Some treatment details or patient characteristics were not studied. Second, other insurance systems such as the government insurance system were not included. Finally, long-term outcomes were not evaluated.

In conclusion, the rt-PA treatment in acute ischemic stroke patients with the UHC had benefit on discharge status. Some complications of stroke or the rt-PA treatment were significantly higher than no rt-PA treatment.

What is already known on this topic?

An intravenous recombinant tissue plasminogen activator (rt-PA) therapy is beneficial in acute ischemic stroke patients showed by several studies including several Thai studies. However, there are limited data on the national database in this issue.

What this study adds?

An intravenous recombinant tissue plasminogen activator (rt-PA) therapy improved discharge status of acute ischemic stroke patients by the national database. The mortality rate was not different from the stroke care without the rt-PA treatment.

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Potential conflicts of interest

The authors declare no conflicts of interest.

Table 2. Outcomes of acute ischemic stroke patients who registered in the universal coverage database from October 1, 2011 to September 30, 2014 categorized by recombinant tissue plasminogen activator therapy (rt-PA)

Factors	No rt-PA (n = 241,930)	rt-PA (n = 2,102)	*p*-value
Stroke severity			
Intubation	28,769 (11.9)	317 (15.1)	<0.001
Craniotomy/craniectomy	1,115 (0.5)	53 (2.5)	<0.001
Tracheostomy	3,616 (1.5)	61 (2.9)	<0.001
Discharge status			
Death	16,466 (6.9)	126 (6.0)	0.151
Improved	204,845 (85.3)	1,863 (88.7)	<0.001
Complete recovery	868 (0.4)	16 (0.9)	0.005
Not improved	18,031 (7.5)	93 (4.4)	<0.001
Complications			
Decubitus ulcer	2,515 (1.0)	13 (0.6)	0.064
Pneumonia	11,669 (4.8)	155 (7.4)	<0.001
Urinary tract infection	11,715 (4.8)	112 (5.3)	0.307
Pulmonary embolism	70 (0.1)	1 (0.1)	0.459
Status epilepticus	632 (0.3)	6 (0.3)	0.828
Septicemia	8,134 (3.4)	58 (2.8)	0.015
Deep vein thrombosis	329 (0.1)	9 (0.4)	0.003
Gastrointestinal (GI) bleeding	3,436 (1.4)	53 (2.5)	<0.001
GI bleeding with blood transfusion	959 (0.4)	18 (0.9)	0.003
Intracerebral hemorrhage	1,432 (0.6)	131 (6.2)	<0.001

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การรักษาด้วย rt-PA ในผู้ป่วยโรคหลอดเลือดสมองชนิดขาดเลือดเฉียบพลัน: ฐานข้อมูลระดับชาติ

เอกวิทย์ ตันประดิษฐ์, นิศา วรสูต, นรงฤทธิ์ เกษมทรัพย์, สมศักดิ์ เทียมเก่า, กิตติศักดิ์ สวรรยาวิสุทธิ์, กรรณิการ์ คงบุญเกียรติ

วัตถุประสงค์: เพื่อประเมินผลการรักษาด้วยยา recombinant tissue plasminogen activator (rt-PA) ทางหลอดเลือดดำในผู้ป่วยโรคหลอดเลือดสมองชนิดขาดเลือดเฉียบพลันจากฐานข้อมูลระดับชาติ

วัสดุและวิธีการ: การศึกษานี้เป็นการศึกษาแบบย้อนหลัง (retrospective analytical study) ฐานข้อมูลได้จากสำนักงานหลักประกันสุขภาพแห่งชาติ (สปสช.) ในประเทศไทย ข้อบ่งชี้ในการรับเข้าการศึกษาคือผู้ป่วยผู้ใหญ่ที่ได้รับการวินิจฉัยเป็นโรคหลอดเลือดสมองชนิดขาดเลือดเฉียบพลันที่ได้รับการรับเข้านอนโรงพยาบาลตามลำดับ การศึกษานี้ใช้ข้อมูลตั้งแต่วันที่ 1 ตุลาคม พ.ศ. 2547 ถึง วันที่ 30 กันยายน พ.ศ. 2556 โดยเปรียบเทียบผลการรักษา ภาวะแทรกซ้อนระหว่างกลุ่มที่ได้รับและไม่ได้รับยา rt-PA

ผลการศึกษา: ในช่วงเวลาที่ทำการศึกษาพบว่ามีผู้ป่วยเข้าข้อบ่งชี้ของการศึกษา 244,032 ราย โดย 2,102 ราย (ร้อยละ 0.9) ได้รับยา rt-PA กลุ่มที่ได้รับ rt-PA มีสถานะก่อนออกจากโรงพยาบาล (discharge status) ดีกว่ากลุ่มที่ไม่ได้รับยา rt-PA อย่างมีนัยสำคัญ ยกเว้นการเสียชีวิต (ร้อยละ 6.9 กับ ร้อยละ 6.0; ค่า $p = 0.151$) มีภาวะแทรกซ้อน 6 รายการที่ต่างกันอย่างมีนัยสำคัญระหว่างทั้งสองกลุ่ม โดยกลุ่มที่ได้ยา rt-PA มีอัตราการเกิดภาวะแทรกซ้อนห้ารายการที่สูงกว่ากลุ่มไม่ได้ยา rt-PA โดยกลุ่มที่ไม่ได้ยา rt-PA มีเพียงการเกิดการติดเชื้อในกระแสเลือดที่สูงกว่ากลุ่มที่ได้ยา rt-PA (ร้อยละ 3.4 กับ ร้อยละ 2.8; ค่า $p = 0.015$)

สรุป: การรักษาด้วยยา rt-PA ในผู้ป่วยโรคหลอดเลือดสมองชนิดขาดเลือดเฉียบพลันจากฐานข้อมูลสปสช. พบว่ามีประโยชน์ต่อผลการรักษา มีภาวะแทรกซ้อนบางอย่างในกลุ่มที่ได้รับการรักษาด้วยยา rt-PA สูงกว่ากลุ่มที่ไม่ได้รับยา rt-PA อย่างมีนัยสำคัญ