Original Article

Is Computed Tomography of the Brain Necessary after Thrombolytic Therapy in Acute Ischemic Stroke?

Julanon N, 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

Acute ischemic stroke is a public health issue worldwide. Currently, the effective treatment for acute ischemic stroke is an intravenous recombinant tissue plasminogen activator (rt-PA). The follow-up CT brain after the rt-PA is still controversial. This study was a retrospective study with an aim to evaluate roles of CT brain after rt-PA treatment. The inclusion criteria were all consecutive adult patients diagnosed as acute ischemic stroke who received the rt-PA. The patients were categorized into two groups by the presence of the follow-up CT brain. For those who performed the CT brain, results of the CT brain or management were correlated with clinical status at 24 hours after the rt-PA and stroke types. There were 211 eligible patients. Of those, 86 patients (40.76%) performed the CT brain after the rt-PA treatment within 24 to 36 hours. For the CT brain group, hemorrhagic transformation occurred the highest in those without clinical improvement with the NIHSS at 24 hours over 10 (14/32 patients; 43.75%). The overall hemorrhagic transformation was 23 patients (26.74%). Regarding stroke type, the intracerebral hemorrhage was found mostly in large arterial stroke (16 patients). While, the malignant middle cerebral artery infarction was found in seven patients (8.14%); five patients with large arterial stroke and two patients with cardioembolic stroke. In conclusion, the follow-up CT brain after the rt-PA treatment may be performed in selected cases such as those without clinical improvement with the NIHSS of over 10 or large arterial/cardioembolic stroke.

Keywords: Hemorrhagic transformation, rt-PA, Middle cerebral artery infarction

Acute ischemic stroke is a public health issue worldwide. The prevalence of acute ischemic stroke in the United States people with those age over 20 years was approximately seven million patients with an incidence of new onset or recurrent stroke of 795,000 patients per year[1]. Currently, the effective treatment for acute ischemic stroke is an intravenous recombinant tissue plasminogen activator (rt-PA) within 4.5 hours of stroke onset[2,3]. Those patients who received the rt-PA treatment had higher chance of complete recovery at three months compared with placebo (50% vs. 38%).

The main issue of the rt-PA treatment is intracerebral hemorrhage or hemorrhagic transformation. The intracranial bleeding is usually occurred between 24 to 36 hours after the rt-PA treatment with the prevalence between 6.4% to 11.8%[3-5]. Even though a computed tomography (CT) of the brain may be needed after the rt-PA treatment, a study from Thammasart University found that the follow-up CT of the brain may not be necessary[6]. The follow-up CT brain did not affect the management plan in 85% of patients with the NIH Stroke Scale (NIHSS) of less than 10 at 24 hours after the rt-PA treatment. However, the study concluded the necessity of the CT brain after the rt-PA treatment based in only 200 patients. This study, therefore, aimed to add knowledge and numbers of patients to this issue.

Materials and Methods

The present study was a retrospective study and conducted at Srinagarind Hospital, Khon Kaen University. The study period was between May 2008 and April 2012. The inclusion criteria were all consecutive adults patients diagnosed as acute ischemic stroke who received the rt-PA treatment.

Baseline characteristics of all eligible patients were recorded from the medical record. The patients were categorized into two groups by presence of the follow-up CT brain after the rt-PA treatment within 24 to 36 hours. Clinical factors were compared between both groups by descriptive statistics. For those who performed the CT brain, results of the CT brain or management were correlated with the clinical status at 24 hours after the rt-PA treatment and stroke types. Clinical status at 24 hours after the rt-PA

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

treatment was categorized into six groups as follows: complete improvement or NIHSS was zero, early improvement with the NIHSS at 24 hours of 1 to 4, early improvement with the NIHSS at 24 hours of 5 to 10, early improvement with the NIHSS at 24 hours of more than 10, no clinical improvement with the NIHSS at 24 hour of 10 or lower, and no clinical improvement with the NIHSS at 24 hours of more than 10. The stroke types comprised of large arterial stroke, lacunar stroke, cardioembolic stroke, and undermined.

Stroke outcomes were also evaluated in all eligible patients including disability by modified Rankin Scale (mRS) of two or lower, improvement of NIHSS score at discharge day compared with admission day, and the 3-month mortality rate. These outcomes were compared between the CT brain and no CT brain groups.

Results

During the study period, there were 211 eligible patients. Of those, 86 patients (40.76%) performed the CT brain after the rt-PA treatment within 24 to 36 hours. Clinical factors between both groups were shown in Table 1. The CT brain group had higher proportions of atrial fibrillation, valvular heart disease, previous stroke, large arterial stroke,

and cardioembolic stroke than the no CT brain group. The NIHSS score of the CT brain group also higher than the no CT brain group in terms of baseline NIHSS (13.09 vs. 8.31), 24 hours after rt-PA NIHSS (12.78 vs. 3.97), and NIHSS at discharge day (11.56 vs. 3.69). For the Barthel index, the CT brain group had lower score at admission (39.04 vs. 57.02) and at discharge day (45.72 vs. 78.51) than the no CT brain group.

For the CT brain group (Table 2), hemorrhagic transformation occurred in highest in those without clinical improvement with the NIHSS at 24 hours over 10 (14/32 patients; 43.75%). The overall hemorrhagic transformation was 23 patients (26.74%). The malignant middle cerebral artery infarction was found in 8 patients (9.30%). Only one patient (1.16%) developed cerebellar infarction.

Regarding stroke type, the intracerebral hemorrhage was mostly in a large arterial stroke (16 patients) as shown in Table 3. While, the malignant middle cerebral artery infarction was found in seven patients (8.14%); five patients in large arterial stroke and two patients in cardioembolic stroke.

The CT brain group had poorer stroke outcomes at three months compared with the no CT brain group in terms of modified Rankin score, NIHSS score, and mortality

Table 1. Baseline characteristics and outcomes of acute ischemic stroke patients who treated with an rt-PA and categorized by follow-up computed tomography (CT) of the brain at 24 hours after treatment (n = 211)

Factors	CT brain (n = 86)	No CT brain (n = 125)
Female	38 (44.19%)	51 (40.80%)
Age (year, mean ± SD)	64.03±15.00	64.20±13.60
Hypertension	46 (53.49%)	64 (51.20%)
Dyslipidemia	15 (17.44%)	29 (23.20%)
Diabetes mellitus	30 (34.88%)	26 (20.80%)
Coronary artery disease	6 (6.98%)	16 (12.80%)
Congestive heart failure	5 (5.81%)	3 (2.40%)
Atrial fibrillation	22 (25.58%)	17 (13.60%)
Valvular heart disease	9 (10.47%)	7 (5.60%)
Peripheral arterial disease	1 (1.16%)	1 (0.80%)
Transient ischemic attack	1 (1.16%)	9 (7.20%)
Prior ischemic stroke	9 (10.47%)	7 (5.60%)
Current smoking[a]	35 (41.18%)	58 (46.40%)
Current alcohol drinking[a]	38 (44.19%)	53 (42.40%)
Pre-stroke mRS[b] = 0	75 (87.21%)	116 (92.80%)
Onset-to-needle time (minute, mean ± SD)	193.71±66.84	190.02±68.41
NIHSS[c] on admission (mean ± SD)	13.09±6.40	8.31±4.93
Barthel index on admission (mean ± SD)	39.04±24.83	57.02±27.22
Normal CT brain on admission	16 (18.60%)	40 (32.00%)
Hyperdense arterial sign in CT brain on admission	22 (25.58%)	40 (32.00%)
Large arterial stroke	44 (51.16%)	42 (33.60%)
Lacunar stroke	26 (30.23%)	63 (50.40%)
Cardioembolic stroke	14 (16.27%)	18 (14.40%)
NIHSS 24 hr after rtPA (mean ± SD)	12.78±8.48	3.97±4.51
NIHSS on discharge day (mean ± SD)	11.56±8.78	3.69±4.72
Barthel index on discharge day (mean ± SD)	45.72±31.29	78.51±28.87

Data presented as numbers (percentage) unless otherwise indicated.
[a] Current smoking/alcohol drinking: within the past six months prior to acute stroke, [b] Modified Rankin scale, [c] National Institutes of Health Stroke Scale

rate (Table 3). The CT brain group had mortality rate of 30.23% which was significantly higher than the no CT brain group (5.6%; *p*-value <0.001).

Discussion

Those acute ischemic stroke patients who received the rt-PA treatment and underwent the follow-up CT brain at 24 hours had poorer prognosis than the no CT brain group (Table 1 and 4). The NIHSS score, Barthel index, and mRS showed less improvement in the CT brain group than the no CT brain group. A previous study showed that those with advanced age, more neurological deficit, or hyperglycemia are at risk for bleeding from the rt-PA therapy[7]. This study found similar findings in terms of more severe neurological deficit but not age (Table 1). The mean age of those with CT brain and without CT brain were comparable (64.03 vs. 64.20 years) as shown in Table 1. But, the glucose level was not evaluated in our study.

The results of this study were comparable with the previous study[6]. Out of 86 patients, there was no management change in regards to clinical status at 24 hours (54/86; 62.79%) or stroke type (53/86; 61.63%) as shown in Tables 2 and 3, respectively. For those with early clinical improvement with the NIHSS lower than 10, there was no change in management in 14/18 patients (77.78%) which was comparable with the previous study (85%). The follow-up CT brain at 24 hours after may be crucial if the clinical status had not improved with the NIHSS over 10. This setting may have risk of hemorrhagic transformation in 43.75% of patients (Table 2). Additionally, a large arterial stroke may increase the risk of malignant middle cerebral artery infarction which needs further intervention (Table 3). The cardioembolic stroke was another setting that may require the follow-up CT brain after the rt-PA treatment from both intracerebral hemorrhage or malignant middle cerebral artery infarction[8].

There are some limitations in this study. First, this study conducted as a retrospective study. Further studies with a randomized controlled trial fashion may be needed to confirm the results of this study. Lastly, the sample size of the present study was still small.

Table 2. Correlation of the results of the follow-up computed tomography of the brain at 24 hours after rt-PA treatment in acute ischemic stroke patients and clinical status (n = 86)

CT result of the patients within 24 h after rtPA treatment	Numbers of the patients evaluated by NIHSS at 24 h after rtPA treatment					
	NIHSS at 24 hr 0 (n = 8)	Early improvement, NIHSS at 24 hr 1 to 4 (n = 6)	Early improvement, NIHSS at 24 hr 5 to 10 (n = 12)	Early improvement, NIHSS at 24 hr >10 (n = 18)	No clinical improvement, NIHSS at 24 hr ≤10 (n = 10)	No clinical improvement, NIHSS at 24 hr >10 (n = 32)
No change management	8 (100%)	5 (83.33%)	9 (75.00%)	8 (44.44%)	8 (80.00%)	16 (50.00%)
Hemorrhagic transformation	0	0	3 (25.00%)	5 (27.78%)	1 (10.00%)	14 (43.75%)
Malignant MCA infarction	0	0	0	5 (27.78%)	1 (10.00%)	2 (6.25%)
Cerebellar infarction	0	1 (16.67%)	0	0	0	0

Table 3. Correlation of the results of the follow-up computed tomography of the brain at 24 hours after rt-PA treatment in acute ischemic stroke patients and stroke types (n = 86)

CT brain results/management	Large arterial stroke (n = 44)	Lacunar stroke (n = 25)	Cardioembolic stroke (n = 13)	Undetermined (n = 3)
No change management	22 (50.00%)	22 (88.00%)	7 (53.85%)	2 (66.67%)
Intracerebral hemorrhage	16 (36.36%)	3 (12.00%)	4 (30.77%)	0
Malignant middle cerebral artery infarction	5 (11.36%)	0	2 (15.38%)	1 (33.33%)
Cerebellar infarction	1 (2.27%)	0	0	0

Table 4. Stroke outcomes between those who underwent and not underwent the follow-up computed tomography of the brain at 24 hours after rt-PA treatment in acute ischemic stroke patients (n = 211)

Factors	CT brain (n = 86)	No CT brain (n = 125)	*p*-value
mRS ≤2 on discharge day	16 (18.60%)	79 (63.20%)	<0.0001
Improved NIHSS on discharge day	50 (58.14%)	106 (85.48%)	<0.0001
Mortality rate at 3 months	26 (30.23%)	7 (5.6%)	<0.0001

In conclusion, the follow-up CT brain after the rt-PA treatment may be performed in selected cases such as those without clinical improvement with the NIHSS of over 10 or large arterial/cardioembolic stroke. Further large and randomized controlled trial may be needed.

What is already known on this topic?

The follow-up CT scan of the brain in acute ischemic stroke patients who received thrombolytic therapy is controversial.

What this study adds?

The follow-up CT brain after the rt-PA treatment may be performed in selected cases such as those without clinical improvement with the NIHSS of over 10 or large arterial/cardioembolic stroke.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การส่งตรวจเอกซเรย์คอมพิวเตอร์สมองหลังจากการรักษาโรคหลอดเลือดสมองชนิดขาดเลือดด้วยยาละลายลิ่มเลือดมีความจำเป็นหรือไม่

นราชัย จุฬานนท์, นิศา วรสูต, นรงฤทธิ์ เกษมทรัพย์, สมศักดิ์ เทียมเก่า, กิตติศักดิ์ สวรรยาวิสุทธิ์, กรรณิการ์ คงบุญเกียรติ

โรคหลอดเลือดสมองชนิดขาดเลือดเป็นปัญหาทางสาธารณสุขทั่วโลก ปัจจุบันการรักษาโรคหลอดเลือดสมองชนิดขาดเลือดที่ได้ผลดีคือการรักษาด้วยยาละลายลิ่มเลือดหรือ rt-PA การส่งตรวจเอกซเรย์ขอมพิวเตอร์สมองหลังจากการรักษาด้วยยาละลายลิ่มเลือดยังเป็นที่ถกเถียงกัน การศึกษานี้เป็นการศึกษาย้อนหลังที่มีวัตถุประสงค์ที่จะประเมินแนวทางการส่งตรวจเอกซเรย์คอมพิวเตอร์สมองหลังจากการรักษาโรคหลอดเลือดสมองชนิดขาดเลือดด้วยยาละลายลิ่มเลือดโดยมีเกณฑ์คัดเข้าการศึกษาคือผู้ป่วยผู้ใหญ่ที่ได้รับการวินิจฉัยว่าเป็นโรคหลอดเลือดสมองชนิดขาดเลือดและได้รับการรักษาด้วยยาละลายลิ่มเลือด ผู้ป่วยจะถูกแบ่งเป็น 2 กลุ่มตามการได้รับการตรวจเอกซเรย์คอมพิวเตอร์สมอง สำหรับผู้ที่ได้รับการส่งตรวจเอกซเรย์คอมพิวเตอร์สมองจะมีการนำผลของการตรวจเอกซเรย์คอมพิวเตอร์สมองและการรักษาที่เกิดขึ้นจะนำมาสัมพันธ์กับอาการของโรคที่ 24 ชั่วโมงภายหลังจากได้รับยาละลายลิ่มเลือดและชนิดของโรคหลอดเลือดสมอง มีผู้ป่วยเข้าเกณฑ์การศึกษาจำนวน 211 ราย มีผู้ป่วยจำนวน 86 ราย (ร้อยละ 40.76) ที่ได้รับการตรวจเอกซเรย์คอมพิวเตอร์สมองภายหลังจากการรักษาด้วยยาละลายลิ่มเลือดภายใน 24 ถึง 36 ชั่วโมง ผู้ป่วยที่ได้รับการตรวจเอกซเรย์คอมพิวเตอร์สมองพบว่า มีการเกิดเลือดออกสูงสุดในรายที่อาการของโรคไม่ดีขึ้นและมีค่า NIHSS ที่ 24 ชั่วโมงหลังจากการรักษามากกว่า 10 (14 รายจาก 32 รายหรือร้อยละ 43.75) การเกิดเลือดออกในสมองมีทั้งสิ้นจำนวน 23 ราย (ร้อยละ 26.74) พบว่ามีการเกิดเลือดออกสัมพันธ์กับโรคหลอดเลือดสมองชนิดหลอดเลือดแดงใหญ่ตีบจำนวน 16 ราย และมีการเกิดการตีบหรืออุดตันของหลอดเลือดแดง middle cerebral ชนิดรุนแรงจำนวน 7 ราย (ร้อยละ 8.17) โดย 5 รายเกิดในโรคหลอดเลือดสมองชนิดหลอดเลือดแดงใหญ่ตีบและอีก 2 รายเกิดในผู้ป่วยที่เป็นหลอดเลือดสมองอุดตันจากลิ่มเลือดจากหัวใจ โดยสรุป การส่งตรวจเอกซเรย์คอมพิวเตอร์สมองหลังจากการรักษาโรคหลอดเลือดสมองชนิดขาดเลือดด้วยยาละลายลิ่มเลือดควรพิจารณากระทำเป็นกรณี อาทิ ผู้ที่อาการของโรคไม่ดีขึ้นและมีค่า NIHSS ที่ 24 ชั่วโมงหลังจากการรักษามากกว่า 10 หรือเป็นโรคหลอดเลือดสมองชนิดหลอดเลือดแดงใหญ่ตีบหรือจากการมีลิ่มเลือดจากหัวใจไปอุดตันหลอดเลือดสมอง