Original Article

Does Atrial Fibrillation Worsen Stroke Outcomes in Acute Ischemic Stroke Treated with rt-PA?

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Atrial fibrillation (AF) has been shown to worsen clinical outcomes in stroke patients. However, data of stroke outcomes and AF in Thai patients received a recombinant tissue plasminogen activator (rt-PA) are limited. This study was a descriptive retrospective study and conducted at Srinagarind Hospital of Khon Kaen University and other six hospitals in northeastern Thailand. The study period was between May 1, 2008 and April 30, 2013. The inclusion criteria included adult patients diagnosed with acute ischemic stroke who received rt-PA treatment. All eligible patients were divided into two groups by presence of AF. The stroke outcomes included the NIH Stroke Scale (NIHSS), modified Rankin scale (mRS), side effects of rt-PA, complications from stroke, and deaths. All outcomes were evaluated at discharge date. There were 768 patients for the analysis; 177 patients (23.04%) had AF. The AF group had more patients with severe or NIHSS more than 16 than the non-AF group (50.57% vs. 24.23%; *p*-value <0.001). Regarding stroke outcomes, the AF group had fewer patients with favorable clinical outcomes than those without stroke (34.45% vs. 57.88%; *p*-value <0.001), and had higher rate of intracerebral hemorrhage (23.73% vs. 9.60%; *p*-value <0.001) than the non-AF group. There was no significant mortality rate between both groups. In conclusion, Thai acute ischemic stroke with AF were more severe and had worse outcomes than those without AF despite the rt-PA treatment.

Keywords: Complications, Atrial fibrillation, NIHSS

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Atrial fibrillation (AF) is the most common cardiac arrhythmia in Thailand[1]. Acute ischemic stroke is increasing by age and presence of AF[2]. Acute ischemic stroke patients also had poor prognosis if AF is one of the co-morbid disease[3-8]. A previous study found that acute ischemic stroke patients without AF had a 30-day mortality rate at 10.2%. This mortality rate was increased to 22.3% in patients with AF[9]. A study from Thailand also found similar findings; the mortality rate of acute ischemic stroke patients was higher in AF than non-AF group significantly (14.1% vs. 6.2%; *p*-value <0.001) including intracerebral hemorrhage from rt-PA and duration of hospital duration[10].

Currently, thrombolytic therapy by a recombinant tissue plasminogen activator (rt-PA) is a standard treatment for acute ischemic stroke. Several stroke outcomes including functional status or mortality rate were significantly improved if rt-PA was given within 4.5 hours. In Thailand, a study found that half of patients received the rt-PA treatment had complete recovery at 24 hours[11]. Even though there are some reports on stroke outcomes in patients received rt-PA in Thailand[11,12], there is limited data on effects of AF in acute ischemic stroke who received the rt-PA treatment.

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Materials and Methods

The present study was a descriptive retrospective study and conducted at Srinagarind Hospital of Khon Kaen University and other six hospitals in the service area of Public Health section 7 and 8 in northeastern Thailand; Chumpae Hospital, Ubon Ratchathani Hospital, Nakhon Panom Hospital, Chaiyaphum Hospital, Kalasin Hospital, and Nakhon Ratchasima Hospital. The study period was between May 1, 2008 and April 30, 2013. The inclusion criteria included adult patients diagnosed as acute ischemic stroke who received rt-PA treatment. Those with incomplete data were excluded.

All eligible patients were divided into two groups by presence of AF. Baseline characteristics and stroke outcomes of all patients were recorded. The stroke outcomes included the NIH Stroke Scale (NIHSS), modified Rankin scale (mRS), side effects of rt-PA, complications from stroke, and deaths. All outcomes were evaluated at discharge date. Studied variables and outcomes between both study groups were compared by descriptive statistics. All statistical

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analyses were computed by the STATA software version 10.0 (College Station, Texas, USA).

Results

During the study period, there were 806 patients met the study criteria. Of those, 38 patients were excluded due to incomplete data. There were 768 patients for the analysis; 177 patients (23.04%) had AF. Among the baseline characteristics, there were six significant factors between those with and without AF (Table 1) including age, sex, history of congestive heart failure, history of valvular heart disease, history of previous stroke, Baseline NIHSS and CT brain findings. The AF group had older age than those without AF (66.65 vs. 62.98 years), while the non-AF group had higher proportions of male patients (57.24% vs. 44.64%).

Regarding stroke outcomes (Table 2), the non-AF group had higher proportion of patients with NIHSS of 0 to 6 at discharge day than the AF group (87.88% vs. 34.45%; *p*-value <0.001), while the AF group had higher rate of intracerebral hemorrhage (23.73% vs. 9.60%; *p*-value <0.001) and longer admission duration (9.20 vs. 6.36 days; *p*-value = 0.026). The AF group had non-significant higher mortality rate than the non-AF group (7.90% vs. 5.07%; *p*-value = 0.583).

Discussion

As previously reported, the AF group had older aged, more proportions of females, and more previous stroke patients than the non-AF group[2,10]. Presence of hypertension may increase risk of stroke in patients with AF by two times (95% CI of 1.6, 2.5)[2]. This found that stroke patients with AF had more history of hypertension than those without AF but not significantly (53.11% vs. 47.63%; *p*-value = 0.202). These findings may be due to under-diagnosed of hypertension in population. Furthermore, rheumatic heart disease is still prevalent resulting in high prevalence of valvular AF than AF from hypertension or other causes such as obstructive sleep apnea[13].

The correlations between stroke type and mortaliry are still being debated. One study found that cardioembolic stroke had higher mortality rate at 30 days than large arterial disease[14], while another study found that there was no

Table 1. Baseline characteristics of acute ischemic stroke patients receiving an rt-PA treatment categorized by presence of atrial fibrillation (n = 768)

Factors	AF (n = 177)	Non-AF (n = 591)	*p*-value
Age (year)			
≤59 year	47 (26.55%)	216 (37.06%)	0.018
60 to 69	46 (25.99%)	163 (27.58%)	
70 to 79	63 (35.59%)	163 (27.58%)	
≥80	21 (11.86%)	46 (7.78%)	
Male	79 (44.63%)	337 (57.02%)	0.003
Risk factors			
Diabetes mellitus	41 (23.16%)	122 (20.54%)	0.453
Hypertension	94 (53.11%)	283 (47.63%)	0.202
Dyslipidemia	28 (15.82%)	109 (18.35%)	0.439
Coronary atery disease	14 (7.91%)	38 (6.4%)	0.481
Congestive heart failure	7 (10.77%)	4 (1.12%)	<0.001
Valvular heart disease	48 (27.12%)	15 (2.53%)	<0.001
Peripheral atery disease	0	2 (0.56%)	0.545
History transient ischemic attack	3 (4.62%)	15 (4.21%)	0.883
Previous stroke	41 (23.16%)	77 (12.98%)	0.001
Smoking	21 (32.82%)	131 (36.9%)	0.105
Previous anticoagulant	6 (3.39%)	4 (0.67%)	0.050
Previous antiplatelet	28 (15.82%)	69 (11.62%)	0.139
No preexisting disability (mRS 0 to 1)	61 (93.85%)	340 (95.77%)	0.889
NIHSS at admission			<0.001
0 to 6 (mild)	9 (5.17%)	123 (21.13%)	
7 to 15 (moderate)	77 (44.25%)	318 (54.64%)	
≥16 (severe)	88 (50.57)	141 (24.23%)	
CT (modified TOAST)			<0.001
Large arterial disease	25 (14.17%)	219 (42.12)	
Lacunar stroke	71 (42.01%)	204 (39.23%)	
Cardioembolic stroke	73 (43.20%)	93 (17.88%)	
Other determine	0	0	
Undetermine	0	4 (0.77%)	

Data presented as number (percentage); AF = atrial fibrillation, NIHSS = National Institutes of Health Stroke Scale, TIA = transient ischemic attack, mRS = modified Rankin scale

significant different on mortality rate and stroke subtype[15]. The present study did not evaluate this correlation but found that there was no significant different mortality (Table 2). The mortality data in the present study were different from previous two studies[7,10]. Both studies showed that stroke patients with AF had significant higher mortality rate than the non-AF stroke patients (14.1% vs. 6.2%; *p*-value <0.001)[10]. These differences may be explained by small sample size in the present study.

Unlike mortality rate, the present study found similar findings with other studies in terms of stroke severity and stroke outcomes in stroke patients with AF[10,16,17]. The AF group had more patients with severe or NIHSS more than 16 than the non-AF group (50.57% vs. 24.23%; *p*-value <0.001) as shown in Table 1. Additionally, the AF group had fewer patients with favorable clinical outcomes or NIHSS between 0 to 6 than those without stroke (34.45% vs. 57.88%; *p*-value <0.001) as shown in Table 2. These findings also found in other outcomes such as more intracerebral hemorrhage from rt-PA treatment and longer duration of hospitalizations (Table 2). All of these findings may be explained from larger cerebral infarction from AF (Table 1).

There are some limitations in the present study. First, there was an issue on determining stroke subtypes according to the modified TOAST criteria. In some patients, it may be difficult to define if it is cardioembolic or a large infarction. Second, all outcomes were evaluated at discharge date. The mortality rate may be higher than reported if evaluation were performed at 30 days after discharge.

In conclusion, Thai acute ischemic stroke patients with AF were more severe and had worse outcomes than those without AF, but not mortality at discharge despite the rt-PA treatment.

What is already known on this topic?

Atrial fibrillation worsened stroke outcomes in acute ischemic stroke patients who received rt-PA treatment. These data are limited in Thai population.

What this study adds?

Atrial fibrillation worsened stroke outcomes in acute ischemic stroke patients who received rt-PA treatment in Thai patients.

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Table 2. Stroke outcomes at discharge and complications of acute ischemic stroke patients receiving an rt-PA treatment categorized by presence of atrial fibrillation (n = 768)

Outcomes	AF (n = 177)	Non-AF (n = 591)	*p*-value
NIHSS			<0.001
0 to 6	49 (34.45%)	290 (57.88%)	
7 to 15	60 (42.55%)	154 (30.74%)	
≥16	32 (22.70%)	57 (11.38%)	
NIHSS improvement	82 (58.99%)	256 (51.61%)	0.123
mRS			0.421
0 to 1 (no disability)	15 (30%)	103 (35.89%)	
2 to 5	35 (70%)	194 (61.11%)	
Deaths	14 (7.9%)	30 (5.07%)	0.583
Causes of deaths			
Intracerebral hemorrhage	6 (42.86%)	14 (46.67%)	
Diffuse brain infarction	7 (50%)	11 (36.67%)	
Others	1 (7.14%)	5 (16.67%)	
Intracerebral hemorrhage	42 (23.73%)	57 (9.6%)	<0.001
Diffuse brain infarction	4 (2.26%)	8 (1.35%)	0.389
Bleeding at other sites	2 (1.12%)	8 (1.35%)	0.598
Other complications			0.873
Sepsis	16 (88.89%)	44 (86.27%)	0.691
Pneumonia	12	34	
Urinary tract infection	4	9	
Pressure sore	0	1	
Seizure	0	2 (3.92%)	
Others	2 (11.11%)	5 (9.8%)	
Mean hospital admission, days	9.20	6.36	0.026

Data presented as number (percentage), unless indicated otherwise; NIHSS = National Institutes of Health Stroke Scale; mRS = modified Rankin scale

Potential conflicts of interest

The authors declare no conflict of interest.

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