

A Comparison of Mechanical Thrombectomy for Large Vessel Occlusion in Acute Ischemic Stroke between Patients with and without Atrial Fibrillation

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ABSTRACT

Objective: Atrial fibrillation (AF) is one of the major risk for large vessel acute ischemic stroke. Mechanical thrombectomy is a promising therapeutic adjunct for large vessel occlusion and also the option for patients who missed the golden time window or who have contraindications for intravenous recombinant tissue plasminogen activator (rtPA). The purpose of this study was to investigate whether AF is a prognostic predictor for the patients with ischemic stroke undergoing mechanical thrombectomy.

Methods: Medical records of all patients with acute ischemic stroke (AIS) caused by large vessel occlusion (LVO) who received mechanical thrombectomy at Siriraj Hospital between November 2009 and November 2016 were retrospectively reviewed. Clinical parameters between the two groups were retrieved and compared.

Results: One hundred and thirty-eight acute ischemic stroke (AIS) patients were treated by endovascular mechanical thrombectomy at Siriraj Hospital between November 2009 and November 2016. Five patients lost from the follow-up process. Totally, 134 patients were included to this study. Fifty patients (37.3%) were in the AF group, 10 patients (7.5%) had a newly diagnosed AF. The AF patients were younger ($p=0.002$) and had less intracranial atherosclerosis ($p=0.015$) than non-AF patients. Nevertheless, gender, mean NIHSS, the mean time from puncture to recanalization, mean onset to recanalization, number of the passing of the stent, TICI, symptomatic intracranial hemorrhage, good clinical outcome at 90 days, and mortality rate were not different between two groups.

Conclusion: There is no significant difference of good outcome and complications between AF and non-AF patients with AIS from LVO who underwent mechanical thrombectomy.

Keywords: Acute ischemic stroke; atrial fibrillation; mechanical thrombectomy (Siriraj Med J 2018;70: 278-283)

INTRODUCTION

In the setting of large vessel occlusion (LVO) with intravenous tissue plasminogen activator (IV-tPA), it is associated with low rate of recanalization and high rate of neurological morbidity and mortality. Mechanical thrombectomy is a promising therapeutic adjunct to IV-tPA for the treatment of acute LVO.

The results of the endovascular treatment for acute

ischemic stroke were proved to reduce disability among patients with ischemic stroke treated with mechanical thrombectomy in addition to standard care.¹

To date, at least five additional endovascular stroke randomized controlled trials; Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE), Extending the time for thrombolysis in

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emergency neurological deficits--intra-arterial (EXTEND-IA), Solitaire with the Intention for thrombectomy as primary endovascular treatment (SWIFT PRIME), Randomized trial of revascularization with solitaire FR device versus best medical therapy in the treatment of acute stroke due to anterior circulation large vessel occlusion presenting within eight hours of symptom onset (REVASCAT) and Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE) were halted prematurely for efficacy.²⁻⁶ Many reports of mechanical thrombectomy showed a significant improvement in the rate of functional independence, with an absolute difference of 8-31 percent.⁷

Atrial fibrillation (AF) is globally considered one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity. Furthermore, the number of patients with AF was predicted to considerably rise in the coming years.⁸ In 2010, the number of men and women with AF worldwide was estimated for 20.9 and 12.6 million people, respectively. Moreover, higher incidence and prevalence would be observed in developed countries.⁹⁻¹⁰ By 2030, 14 – 17 million AF patients were anticipated in the European Union, with 120,000 – 215,000 newly diagnosed patients per year.^{9,11-12}

AF prevalence is approximately 3% in adults aged 20 years or older,¹³⁻¹⁴ with greater prevalence in older persons⁹ and in patients with conditions, such as hypertension, heart failure, coronary artery disease (CAD), valvular heart disease, obesity, diabetes mellitus, or chronic kidney disease.¹⁵⁻²⁰ Moreover, AF is considered an independent risk factor for stroke and increases its incidence nearly 5 folds.²¹ The attributable risk of stroke for AF rises proportional to age, from 1.5% for those aged 50 to 59 years to 23.5% for those aged 80 to 89 years. Furthermore, AF is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men.²²⁻²⁴

In both developed and developing countries, the age-adjusted incidence and prevalence of AF are lower in women, while the risk of death in AF women is similar to or higher than that in AF men.^{9,25} Besides, female AF patients who have additional stroke risk factors (particularly older age) also possess greater risk than men having a stroke, even those anticoagulated with warfarin.²⁶⁻²⁸

Randomized clinical trials in AF showed that an average annual stroke rate was about 1.5% and the annualized death rate was approximately 3% in anticoagulated AF patients.²⁹ The most important risk factors for stroke in patients with AF include advanced age and previous cardioembolic stroke or transient ischemic attack (TIA).³⁰

Moreover, AF is an important risk factor for ischemic stroke, which accounts for approximately 21-37% of the patients with ischemic stroke.³¹

The aim of this study was to investigate whether AF is a prognostic predictor for patients with ischemic stroke undergoing mechanical thrombectomy.

MATERIALS AND METHODS

Medical records of patients visiting Siriraj Hospital with ischemic stroke caused by LVO, together with salvageable tissues from CT perfusion or multiphase CTA and could come to follow up at the hospital by 90 days from November 2009 to November 2016 were retrospectively reviewed. Inclusion criteria were as followed: 1) those who had LVO in anterior circulation stroke within 8 hours with Alberta Stroke Program Early CT Score (ASPECTS) more than 6 points, or collateral score more than 3 points, or mismatched area more than 2/3 of the territory or 2) those who had LVO of posterior circulation stroke without clinical or imaging of brainstem infarction.

The patients, who were eligible, received intravenous-tPA immediately before CT angiography.^{4,6-7} The effect of IV-tPA was not considered to be a criteria of patient selection for mechanical thrombectomy. (comment WU1) In addition, informed consent was signed by individual patients or their family members. However, exclusion criteria were as followed: 1) life expectancy was less than 3 months 2) platelets were less than 30,000/cubic millimeters (mm³) 3) subarachnoid hemorrhage (SAH) or intracranial hemorrhage 4) massive brain edema from any causes 5) history of severe allergy to contrast media 6) clinical-radiographic match 7) extensive brainstem infarction.

Intracranial atherosclerosis was presumed if a residual stenosis of the affected vessel was presented, after recanalization. (comment WU2)

The diagnostic criteria for AF were as followed: P wave disappeared and was replaced by series of atrial fibrillation waves of various size, shape, and interval. Besides, atrial rate was 350-600 beats per minute and had completely irregular ventricular rate. In addition, QRS wave showed supraventricular form or widened deformity. Furthermore, AF was also established for those without f waves but with completely irregular RR intervals.

Statistical analysis; All data were manipulated and analyzed statistically with SPSS (version 21, SPSS Inc., Chicago, Ill., USA). The descriptive data were reported as mean with standard deviation or median with interquartile length and analyzed using unpaired t-test with unequal

variance or Mann-Whitney U test depending on the underlying data distribution. Categorical and dichotomized variables were described as a percentage and analyzed using Fisher's exact test. Unadjusted outcome effect sizes were estimated as differences in mean, median, or odds ratios (OR) with 95% CI as appropriate. $P < 0.05$ was regarded as statistically significant.

RESULTS

One hundred and thirty eight patients with acute ischemic stroke (AIS) were treated by endovascular mechanical thrombectomy at Siriraj Hospital between November 2009 and November 2016. Of those, five patients did not visit the doctor for follow-up. Accordingly, 134 patients were included in this study, with the mean age of 64.2 years old. It consisted of 78 male and 56 female patients. Mean for the National Institutes of Health Stroke Scale (NIHSS) was 17.2. The anterior circulation stroke was found 80%. Intravenous rTPA had indication in 21.6% of patients. Intracranial atherosclerosis disease (ICAD) was documented in 18.7%

The mean time from puncture to recanalization was 94 minutes. The mean time from onset to recanalization was 401 minutes. Symptomatic hemorrhage was found 13.5%. The rate of good recanalization, determine by Thrombolysis in cerebral infarction (TICI) 2B and 3, was 76.1%. The good outcome (modified Rankin scale ≤ 2) at 90 days was found 38.3%. In addition, baseline data, results, and complications between AF and non-AF groups are shown in Table 1.

According to Table 1, age of patients in AF group was significantly older than those in non-AF group ($p=0.002$). In addition, intracranial atherosclerosis disease in AF patients was significantly less than that in AF patients ($p=0.015$). Nevertheless, sex, mean NIHSS, mean time from puncture to recanalization, mean time from onset to recanalization, the number of pass of the stent, TICI, symptomatic intracranial hemorrhage, good clinical outcome at 90 days, and mortality rate were not significantly different between two groups.

In the present study, 10 patients had a newly diagnosed AF (AF was diagnosed at onset of stroke or within 1 week

TABLE 1. Parameters between AF and non-AF patients.

Parameters	Total (N=134)	AF group (N=50)	Non-AF group (N=84)	P value
Age	63.9 $\pm$ 15.5	69.2 $\pm$ 12.9	60.2 $\pm$ 16.0	0.002*
Male sex (n. %)	78 (57.9%)	27 (54%)	51 (60.7%)	0.446
NIHSS score (118 cases)	17.2 $\pm$ 6.0	17.4 $\pm$ 5.5	17.1 $\pm$ 6.3	0.769
IV-tPA (n. %)	29 (21.6%)	10 (20%)	19 (22.6%)	0.722
ICAD (n. %)	25 (18.7%)	4 (8%)	21 (25%)	0.015*
mRS ≤ 2 at 90 day	51 (38.1%)	19 (38%)	32 (38.1%)	0.570
Puncture to recanalization time (min)	93.8 $\pm$ 103.7	109.3	84.5	0.181
Onset-to-recanalization time (min)	400.3 $\pm$ 264.6	358.0	425.4	0.155
Number of pass of stent median (p25 th - p75 th)	2.75	3 (2-4)	2 (1-3.75)	0.103
Symptomatic ICH (n. %)	17 (12.7%)	6 (12%)	11 (13.1%)	0.854
TICI2b,3	102 (76.1%)	38(76%)	64(76.2%)	0.948
mortality rate	26 (19.4%)	10(20%)	16(19%)	0.893
Anterior circulation	107 (80%)	43 (86%)	64(76.2%)	0.355
Posterior circulation	27 (20%)	7(14%)	20(23.8%)	

*Values with $P < 0.05$ are considered statistical significant

during being admitted in hospital) and 40 patients were documented AF, One patient had intracardiac clot and poor outcome after treatment.

In the AF group, the good outcome was found 42.8% (18/42) in patients with good controlled AF, whereas 12.5% (1/8) in patients with uncontrolled AF (p 0.134).

Results of mechanical thrombectomy between patients with anterior and posterior circulation stroke showed no different outcome (p 0.847) in the present study.

DISCUSSION

Presently, in Thailand, the number of people aged 60 years old and over stands at 8 million heads (13% of total population). By 2040, Thailand aging population is expected to 17 million heads (25% of total population); prevalence of AF in Thai population was expected to 3.46%.³²

AF is an important risk factor for ischemic stroke. AF-induced ischemic stroke presented more severe symptoms and poorer prognosis.³³ An AF-induced thrombus was often larger than one resulting from atherosclerosis and had a higher proportion of older thrombus.³⁴ AF was associated with greater volumes of more severe baseline hypoperfusion, leading to higher infarct growth, more frequent severe hemorrhagic transformation, and worse stroke outcomes.³⁵

It has been postulated that patients with AF had less developed cerebral collateral circulation because the

majority did not have concomitant carotid or intracranial large artery stenosis.³⁶ Stroke due to intracranial large artery stenosis have previously been shown to have better collateral circulation than that due to extracranial large artery stenosis, cardio-embolism, and undetermined causes.^{37,38}

In the limited relevant studies, higher probability of poor prognosis and bleeding was found in ischemic stroke patients with AF after intravenous thrombolytic therapy than in those without AF.³⁹⁻⁴⁰ However, an evidence from the Virtual International Stroke Trials Archive (VISTA) showed that the presence of atrial fibrillation had no independent impact on stroke outcome at 90 days. Among patients with atrial fibrillation, baseline severity (median NIHSS) was greater (p=0.001) and age was higher (p=0.001).

From IV-tPA data, the patients who received thrombolysis experienced an advantage in outcomes that were of equal magnitude whether, in the presence or absence of atrial fibrillation, rate of ICH were similar in both AF and non-AF groups.

According to endovascular aspect, data from China were limited as 35 cases enrolled. Of those, they were 10 cases for AF and 25 cases for non-AF groups. That study found similar percentage of good outcome in both groups after treatment. Nonetheless, patients in AF group had higher percentage of recanalization rate than those in non-AF group.⁴¹ (Table 2)

TABLE 2. Factors relevant to good outcome for mechanical thrombectomy.

Parameters		Poor outcome (mRS >2)	Good outcome (mRS < 2)	P value
Age		66.83±14.1	59.10±16.5	0.005*
Mean NIHSS		18.5	15.6	0.010*
IV-tPA		15 (51.7)	14 (48.3)	0.087
ICAD		18 (16.5%)	7 (28%)	0.254
TICI 2b,3		56 (54.9)	46 (45.1)	0.268
Puncture-to-recanalization time (min)		80	64	0.020*
Onset-to-recanalization time (min)		344	315	0.063
Sex	Male (n. %)	51	27	0.105
	Female (n. %)	24	32	
Site	Anterior (n. %)	66 (61.7%)	41 (38.3%)	0.847
	Posterior (n. %)	17 (63%)	10 (37%)	

*Values with P < 0.05 are considered statistical significant

In the current study, it was composed of 50 cases in AF group and 84 cases in non-AF group. We found that good outcome was not significantly different between AF and non-AF groups (38% vs 38.1%, $p=0.991$). However, mean age of patient in AF group was higher than those in non-AF group (69.24 vs 60.70 years, $p.002$). As for sex, NIHSS, receiving IV r-TPA before treatment, site of occlusion, intracranial stenosis, time of operation, number of pass of stent, symptomatic hemorrhage, and good controlled AF, they were not statistically significant between two groups. It meant that AF in AIS patients undergoing mechanical thrombectomy was not associated with a poor outcome.

For posterior circulation stroke, selected patients who remained brain stem tissue and received mechanical thrombectomy had a same good result rate as patients with anterior circulation stroke. This is the surprising data because most data indicated that posterior circulation stroke was associated with very poor outcome. Young age, low NIHSS, and short procedural time were associated with good outcome at 90 days.

CONCLUSION

We supported that endovascular mechanical thrombectomy was beneficial to LVO patients in both AF and non-AF with AIS. Moreover, this approach demonstrated no difference of complications and mortality rate between both groups. The AF patients with AIS was not associated with a poor outcome with mechanical thrombectomy.

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