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Original Article

Is atrial fibrillation a prognostic predictor for patients with acute ischemic stroke treated with thrombectomy?

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Abstract: To investigate whether atrial fibrillation (AF) is a prognostic predictor for patients with ischemic stroke undergoing thrombectomy. Thirty-five cases with ischemic stroke and indicated for thrombectomy were enrolled between January 1 and December 31, 2014. Holter monitoring was used to identify AF. Subsequently 10 cases and 25 cases were enrolled into the AF and the non-AF Group, respectively. Before thrombectomy, the National Institutes of Health Stroke Scale (NIHSS) score and hemorrhage after thrombolysis (HAT) score were obtained. After thrombectomy, coronary angiography revealed recanalization and restenosis; NIHSS score was obtained immediately, 24 h and 36 h following surgery; the modified Rankin Scale (mRS) score was obtained at 3 months after surgery to assess poststroke residual disability. Logistic regression analysis was performed to identify the factors affecting outcome. Recanalization rate was significantly higher in the AF Group than that in non-AF Group treated by thrombectomy (83% *vs.* 20%) and second-line thrombectomy (98% *vs.* 80%), while the residual stenosis rate was lower by thrombectomy (7% *vs.* 30%) and second-line thrombectomy (2% *vs.* 20%) (all $P<0.05$). NIHSS score was not significantly different between the groups ($P>0.05$) and mRS scores indicated similar percentages of good prognosis ($P>0.05$). Regression analysis showed that after adjusting age, sex, weight, blood pressure and underlying diseases, the AF Group had higher recanalization rate ([$P = 0.046$, OR = 1.072 [1.001, 1.148]) and lower residual stenosis rates ($P = 0.027$, OR = 0.919 [0.853, 0.990]). Although ischemic stroke patients may benefit from thrombectomy regardless of AF, AF predicts a higher recanalization rate and lower stenosis rate after surgery.

Keywords: Ischemic stroke, atrial fibrillation, interventional thrombectomy, recanalization rate, stenosis rate

Introduction

The World Health Organization Global Health Observatory data indicate that China had the highest morbidity rates from stroke in the world in 2013, even higher than the United States. The national retrospective sampling survey of death causes in China showed that stroke had become the most common cause of death and had brought huge disease burden to China. Acute ischemic stroke (AIS) is a common type of stroke in a clinical setting and the first-line therapy involves using thrombolytic agents to remove the clot. Nevertheless, due to the limitations of thrombolytic agents in treating acute cerebral infarction, an ultra-early recanalization technique has been proposed to expand the "thrombolytic" concept to "recanalization" therapy. This involves endovascular intervention and in particular mechanical thrombectomy [1].

Atrial fibrillation (AF) is an important risk factor for ischemic stroke, accounting for about 25% of ischemic stroke [2]. Compared with other causes, AF-induced ischemic stroke presents more severe symptoms and poorer prognosis [3]. An AF-induced thrombus is often larger than one resulting from atherosclerosis and has a higher proportion of older thrombus [4]. In the limited relevant studies available, higher probabilities of poor prognosis and bleeding are found in ischemic stroke patients with AF after intravenous thrombolytic therapy than in those without AF [5, 6]. Considering the nature of the thrombus and features of intra- and extra-cranial vessels, we think that embolectomy is more likely to be appropriate for ischemic stroke patients with AF.

However, no data have validated the differences in recovery after mechanical thrombectomy between patients unresponsive to thrombolytic

Table 1. Baseline data for the study population

Items	AF Group (N = 10)	non-AF Group (N = 25)	*P* values
Male sex (n, %)	4 (40.0%)	21 (84.0%)	0.016
Age (means ± *SD*, years)	65.00 ± 8.17	56.64 ± 7.93	0.009
Weight (kg, m)	67.5 (50, 100)	70 (54, 85)	0.506
SBP (mmHg)	155.20 ± 19.50	148.68 ± 19.64	0.381
DBP (mmHg)	95.60 ± 13.62	93.76 ± 12.57	0.705
Fasting blood glucose (means ± *SD*, mmol/L)	7.85 ± 2.54	7.52 ± 2.34	0.714
Diabetes mellitus (n, %)	3 (30.0%)	5 (20.0%)	0.661
Hypertension (n, %)	8 (80.0%)	13 (52.0%)	0.252
TIA (n, %)	0 (0%)	1 (4.0%)	1.000
CHD (n, %)	9 (90.0%)	1 (4.0%)	<0.001
Myocardial infarction (n, %)	2 (20.0%)	0 (0%)	0.076
Heart failure (n, %)	1 (10.0%)	0 (0%)	0.286
Triglyceride (n, %)	3 (30.0%)	8 (32.0%)	0.200
Total cholesterol (n, %)	0 (0%)	2 (8.0%)	1.000
HAT score	4.50 ± 3.03	22.00 ± 7.36	<0.001
History of cigarette smoking (n, %)	3 (30.0%)	15 (60.0%)	0.146
Site of cerebral infarction (n, %)	--	--	0.007
Brain stem	0 (0%)	10 (40.0%)	
Left cerebral hemisphere	4 (40.0%)	10 (40.0%)	
Right cerebral hemisphere	6 (60.0%)	5 (20.0%)	
Infarct size on CT scan (n, %)	--	--	0.590
None	6 (60.0%)	17 (68.0%)	--
<1/3	4 (40.0%)	7 (28.0%)	--
>1/3	0 (0%)	1 (4.0%)	--

Abbreviations: SD = standard deviation, AF = arterial fibrillation, SBP = systolic blood pressure, DBP = diastolic blood pressure, TIA = transient ischemic attack, CHD = coronary heart disease, HAT = hemorrhage after thrombolysis, CT = computed tomography.

therapy with and without AF. Here we assess the predictive role of AF in the prognosis of patients unresponsive to thrombolytic therapy and undergoing mechanical thrombectomy.

Methods

Clinical materials and grouping

In a prospective cohort study, AIS patients were enrolled from Baotou Central Hospital between January 1 and December 31, 2014, with the inclusion criteria as follows: 1) Severe stroke caused by middle cerebral artery occlusion within 12 h or by posterior cerebral artery within 24 h since onset, and the stroke was not indicated for or recanalized by intravenous thrombolytic therapy; 2) Intracranial hemorrhage was excluded as imaged by head computed tomography or magnetic resonance imaging; 3) Severe limb paralysis as defined by the National Institutes of Health Stroke Scale (NIHSS) score [7] greater than or equal to 4; and 4) Informed consent signed by patients or family members. Exclusion criteria: 1) History of intracranial hemorrhage, including suspected subarachnoid hemorrhage; 2) Traumatic brain injury within 3 months of study; 3) Gastrointestinal or urinary tract bleeding within 3 weeks; 4) Major surgery within 2 weeks; 5) Arteriopuncture on incompressible sites within 1 week; 6) Severe cardiac/hepatic/renal dysfunction or diabetes mellitus; and 7) Pregnancy.

Study methods

A total of 35 cases with ischemic stroke were included and monitored with 24 h dynamic electrocardiography to identify 10 cases complicated with persistent AF, classified into the AF Group, and 25 cases without AF, the non-AF Group. The diagnostic criteria for AF were as follows [8]: P wave disappeared and replaced by a series of atrial fibrillation waves (f waves) of

Table 2. Comparison of the thrombectomy treatment in the study population and according to AF

Parameters	Total (N = 35)	AF Group (N = 10)	non-AF Group (N = 25)	*P* values*
NIHSS score				
Before surgery	13.37 ± 4.95	15.20 ± 4.57	12.64 ± 4.99	0.170
Immediately after surgery	13.23 ± 7.86	17.80 ± 9.65	11.40 ± 6.36	0.027
24 h after surgery	14 (0, 34)	15 (2, 34)	10.5 (0, 34)	0.086
36 h after surgery	10.29 ± 7.85	14.14 ± 7.82	9.00 ± 7.60	0.136
3-month MRS score	1 (0, 3)	1.5 (0, 3)	1 (0, 30)	0.378
HAT score	1 (0, 4)	1 (0, 3)	1 (0, 4)	0.418
Onset-to-intervention time (h)	6.21 ± 3.54	5.40 ± 1.35	6.54 ± 4.08	0.397
Recanalization rate (%)		--	--	--
Thrombectomy	40% (0%, 100%)	83% (0%, 100%)	20% (0%, 100%)	0.011
Second-line thrombectomy	100% (0%, 100%)	98% (0%, 100%)	80% (0%, 100%)	0.023
Residual stenosis rate		--	--	--
Thrombectomy	20% (0%, 100%)	7% (0%, 60%)	30% (0%, 100%)	<0.001
Second-line thrombectomy	0% (0%, 100%)	2% (0%, 10%)	20% (0%, 100%)	0.023
Rebleeding (n, %)	10 (28.6%)	7 (70.0%)	3 (12.0%)	0.002
Reocclusion (n, %)	9 (25.7%)	0 (0%)	9 (36.0%)	0.036
Death (n, %)	10 (28.6%)	4 (40.0%)	6 (24.0%)	0.421

Abbreviations: AF = arterial fibrillation, HAT = hemorrhage after thrombolysis. *compared between AF and non-AF groups.

various size, shape and interval; atrial rate 350-600 beats per minute and completely irregular ventricular rate; QRS wave showing supraventricular form or widened deformity. AF was also established for those without f waves but with completely irregular RR intervals.

All patients were assessed for the severity of stroke with NIHSS score and for the risk of intracranial hemorrhage with HAT score before embolectomy [9]; NIHSS score was also obtained immediately, 24 h and 72 h after the interventional thrombectomy; MRS score was obtained 3 months after thrombolytic therapy [10] to divide the patients into either Good Prognosis Group (0-2 points) or Poor Prognosis Group (3-5 points) according to functional independence level.

Thrombectomy methods

The first-line method of treatment for the patients was mechanical thrombectomy. A radiography exam was applied to ensure the vessel was recanalized. If not, the thrombectomy was repeated up to 3 times for each patient. If the procedure was still not successful, second-line thrombectomy was performed involving balloon dilatation, arterial thrombolysis or stent implantation.

Statistical analysis

Measurement data were tested for normality and homoscedasticity, and then data of normal and non-normal distribution were expressed as mean ± standard deviation (SD) and median (range), respectively. Normally distributed and homoscedastic data (e.g., age, systolic blood pressure [SBP], diastolic blood pressure [DBP]) were compared using *t* test, non-normally distributed data (e.g., weight, HAT score) using nonparametric Wilcoxon signed-rank test, and categorical parameters (e.g., sex, hypertension, diabetes mellitus) using Chi-squared test, with $P<0.05$ defined as significant difference. All significantly different variables as indicated by univariate analysis were further tested with regression model and the factors affecting the recanalization rate and stenosis rate of interventional thrombectomy were analyzed using the forward method of Logistic regression analysis.

Results

Baseline data

The baseline data are presented in **Table 1**. The AF Group had significantly fewer males ($P = 0.016$), more advanced age ($P = 0.009$), more

Table 3. Logistic regression analysis

Parameters	*P* values	OR	95% CI for OR	
			Lower	Upper
Site of cerebral infarction	0.164	41.428	0.220	7811.308
Recanalization rate after thrombectomy	0.046	1.072	1.001	1.148
Residual stenosis rate after thrombectomy	0.027	0.919	0.853	0.990

Table notes: Inclusion factors encompassed sex, age, site of cerebral infarction, infarct size on CT scan, onset-to-intervention time, recanalization rate after thrombectomy, residual stenosis rate after thrombectomy, recanalization rate after second-line thrombectomy and residual stenosis rate after second-line thrombectomy.

coronary heart diseases (CHD, $P<0.001$) and lower HAT score ($P<0.001$), whereas weight, blood pressure, blood glucose and blood lipids were not significantly different between the two groups.

Evaluation of stroke treatment

Repeated measures analysis of variances (general linear model) was employed to compare the NIHSS scores of before, immediately, 24 h and 72 h after surgery between the two groups, which revealed no significant differences (**Table 2**). Nevertheless, compared with the non-AF Group, the AF Group showed a higher recanalization rate for patients treated by thrombectomy (83% *vs.* 20%, $P = 0.011$) and second-line thrombectomy (98% *vs.* 80%, $P = 0.023$) and lower residual stenosis rate for thrombectomy (7% *vs.* 30%, $P<0.001$) and second-line thrombectomy (2% *vs.* 20%, $P = 0.023$) and reocclusion rate (0% *vs.* 36%, $P = 0.036$), but higher rebleeding rate (70% *vs.* 12%, $P = 0.002$). The mortality rates at 28.6% overall had a trend to be higher in the AF Group but this was not found to be statistically significant.

Logistic regression analysis

The results of the logistic regression analysis are shown in **Table 3**. This showed that after adjusting for age, sex, weight, blood pressure and underlying diseases, the AF Group had higher recanalization ($P = 0.046$, OR = 1.072 [1.001, 1.148]) and lower residual stenosis rates ($P = 0.027$, OR = 0.919 [0.853, 0.990]).

Discussion

The aim of this study was to investigate whether AF is a prognostic predictor for patients with ischemic stroke undergoing thrombectomy. The results showed an unsatisfied clinical outcome by mechanical thrombectomy that the total recanalization rate after thrombectomy was only 40% in all cases, especially in those without AF, which was 20%. Residual stenosis rates for second-line thrombectomy and thrombectomy were 20% and 30% in non-AF group, much higher than that in AF Group (2% and 7%). Multivariate regression analysis indicated AF was associated with a higher recanalization rate and lower residual stenosis rate but higher risks for rebleeding.

The recanalization rates in this study of 40% in total and 20% in non-AF patients are disappointing when compared to a recent study [11]. Patients treated with thrombolysis showed rates are as high as 58% [11]. However, in patients not treated by thrombolysis the rate of recanalization was found to be 38% [11]. Therefore, because of the selection of the patients in this study was those not indicated for thrombolysis the recanalization rates might be expected to be lower. That study [11] also found an increased rate of recanalization was associated with AF in agreement with this study. Another recent study achieved higher rates of recanalization even in patients treated with mechanical thrombectomy of 55% [12], although the numbers of patients evaluated was quite small so this may have introduced some bias into the results. A large multicenter study shows that endovascular thrombectomy is progressively improving outcomes over time as the method develops [13]. It is evident that as the techniques improve the recanalization rates will also improve. The time to achieve recanalization with thrombectomy from the onset of symptoms has been shown to have a significant effect upon the prognosis of patients [14], therefore, it is critical to achieve recanalization as quickly as possible. This might be another reason that the recanalization rates are low in the current study, as most of them went through a thrombolytic therapy before included.

The higher rates of residual stenosis in patients without AF suggest that there are complicating factors for using mechanical thrombectomy in these patients. This could be the result of differences in the thrombus between patients with and without AF in terms of size and con-

stituents [4], or other complicating factors resulting in the failure of thrombolysis and thrombectomy in these patients.

As these results show that patients with AF showed higher recanalization and lower residual stenosis rates than patients without AF, they suggest that mechanical thrombectomy is a suitable treatment method that is effective and feasible in a proportion of patients that are not effectively treated with first-line thrombolysis. However, the higher rate of rebleeding is a complication that may have serious implications. It is unclear whether this higher rate was due to the methods of thrombectomy used in this study and further investigation is needed to reveal this and find ways of reducing it. Although mortality rate differed between AF Group and non-AF Group, the difference was not significant, indicating potential biases resulted from a small sample size which should be validated by a larger sample size in the future.

This study has some limitations. Our study had a small sample size and short follow-up period. Moreover, data might have been missed due to the lack of information about secondary cerebral infarction, long-term mortality rate, proportion of patients with successful thrombolytic therapy. We did not include the AF patients undergoing thrombectomy as initial treatment, or compared with those undergoing thrombectomy after thrombolytic therapy.

Conclusion

Ischemic stroke patients may benefit from interventional thrombectomy regardless of AF, but those complicated with AF have a higher recanalization rate and lower stenosis rate after the surgery.

Disclosure of conflict of interest

None.

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