FACTORS RELATING TO GOOD OUTCOMES AFTER MECHANICAL THROMBECTOMY FOR ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE WITHIN 4.5 HOURS FROM THE ONSET

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Mechanical thrombectomy (MT) has been accepted as a standard treatment worldwide for patients suffering from acute anterior large vessel occlusion (AC-LVO) who can start early MT within 6 hours. However, in Vietnam, there remains a paucity of information regarding factors that can affect outcomes following this treatment. This study aimed to assess the clinical, imaging, and procedural factors related to good outcomes after MT for patients with AC-LVO within 4.5 hours. We analyzed data from 120 patients at Bach Mai hospital who had acute ischemic stroke (AIS) due to AC-LVO and were treated with MT with and without intravenous thrombolysis (IVT) within 4.5 hours from December 2020 to September 2022. Logistic regression analysis was used to examine the associations of clinical, imaging, and procedural variables with a good outcome. Overall, successful revascularization was achieved in 102/120 cases (85.0%) and 70 patients (58.3%) had a good outcome at 90 days. Successful revascularization (OR, 1.40; 95% CI, 1.24-1.58; p<0.01), initial blood glucose level (OR, 0.86; 95% CI, 0.85-0.87; p=0.046), and hemorrhagic transformation (OR, 0.83; 95% CI, 0.76-0.90; p=0.02) were independent factors associated with good outcome at 90 days.

Keywords: Acute ischemic stroke, anterior large vessel occlusion, predictive factors, outcome, mechanical thrombectomy, intravenous thrombolysis.

I. INTRODUCTION

Stroke remains a major cause of disability and mortality worldwide despite substantial advances in both prevention and treatment in recent years.[1] In Vietnam, acute ischemic stroke (AIS) due to large vessel occlusion (LVO) is one of the most common causes of disability, hospitalization, and high costs to healthcare and society.[2] More research is needed to prevent AIS as well as to develop more effective treatment methods.

Until now, reperfusion therapy using intravenous thrombolysis (IVT) with tissue plasminogen activator (tPA) and endovascular interventions such as mechanical thrombectomy (MT) are the only the few approved treatments for AIS. For nearly 20 years, IVT has been the sole treatment option for AIS within 4.5 hours of onset.[3] However, this therapy has two major drawbacks: low recanalization rate in LVO (only 10-30%) and increased risk of intracranial hemorrhage (ICH).[3,4] MT was developed to address these problems. The evidence behind the effectiveness of MT as treatment for anterior circulation LVO stroke is clear and unequivocal with 5 randomized controlled trials (RCTs) demonstrating substantial benefits over then best medical therapy.[5] Since, the treatment paradigm for AIS caused by LVO has shifted to MT taking the dominant role.

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In the past few years, there have been significant improvements in device technology and protocols leading to the decrease in time to treatment of MT. As such, there is a global debate regarding the the use of IVT before MT in patients experiencing AC-LVO within 4.5 hours of onset and who are admitted to hospitals capable of performing direct MT. To answer this question, six RCTs comparing treatment with MT alone and treatment combining IVT and MT have been conducted in the world and one clinical trial has been conducted in Vietnam.[6,7] However, a major issue remains as to identifying decision-making arguments for patients likely to benefit from thrombectomy in the early window of 4.5 hours from the onset. Although there exist several studies that investigated prognostic factors that predict outcomes after thrombectomy, these studies were conducted in patients treated with only stent retriever and focused on the larger time window (within 6 hours from onset).[8-11] In Vietnam, MT has been performed since 2012 with both stent retriever and aspiration tubing but there are little information regarding factors associated with good outcomes after MT in patients with AC-LVO. This study aimed to assess the clinical, imaging, and procedural factors associated with good outcome after MT within 4.5 hours of onset in Vietnam.

II. MATERIALS AND METHODS

1. Patients and variables

This prospective, descriptive research was conducted at Bach Mai hospital, the largest and most comprehensive stroke center in northern Vietnam. From December 2020 to September 2022, patients who had AIS caused by anterior circulation large vessel occlusion (AC-LVO) and were treated with MT within 4.5 hours of onset were recruited to participate in the study.

Patients were included if they:

1) were aged ≥18 years,

2) presented with clinical manifestations of AIS, with National Institutes of Health Stroke Scale (NIHSS) score ranging from 6 to 24 points,

3) presented with occlusion of the internal carotid artery (ICA) or the M1 or M2 segment of the middle cerebral artery (MCA) on computed tomography angiography (CTA) or magnetic resonance angiography (MRA);

4) presented with an Alberta Stroke Program Early Computed Tomography (CT) Score (ASPECTS) ≥ 7;

5) satisfied indications for IVT and MT;

6) underwent groin puncture within 4.5 hours of stroke onset; and

7) had the signed informed consent from their representative. Subjects were excluded if they:

a) presented with any contraindication to IVT or

b) were diagnosed with a severely disabling condition (modified Rankin Scale [mRS] > 2).

The clinical variables recorded were age, gender, baseline NIHSS score, and the etiology of stroke. The imaging variables were baseline ASPECTS on nonenhanced CT (NECT) or diffusion-weighted imaging (DWI), and occlusion site (ICA, M1, M2, or tandem occlusion) on CTA or MRA. The variables on the intervention were time to endovascular treatment, procedure time, time to reperfusion, type of anesthesia, number of passages, use of rescue therapy, and any perforation/dissection complications. The outcome variables were success of reperfusion at the end of the procedure according to the thrombolysis in cerebral infarction scale (TICI), intracranial hemorrhage (ICH), and functional outcome at 3 months post-treatment. Successful reperfusion was defined as TICI grade 2b or 3.

Symptomatic ICH (sICH) was defined using the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria.[12] Good outcome was defined as having mRS from 0 to 2 at 3 months follow-up.

2. Treatment procedure

Eligible patients were treated with IVT and/ or MT according to the 2018 American Heart Association/ American Stroke Association guidelines.[13] IVT was done with infusion with a standard dose of 0.9 mg alteplase per kg body weight (maximum dose of 90mg).

Endovascular therapy was performed by an experienced neuro interventionalist under a DSA monoplane (Philips Allura Xper FD20) or a DSA biplane (Philips Allura Xper FD10/10). The type of anesthesia was conscious sedation or general anesthesia. To locate the occlusion site, a large long-sheath (Neuron Max 088, Penumbra Inc, USA) was placed in the carotid artery for angiography. Thrombectomy was performed with a second-generation stent retriever (Solitaire stent, Medtronic, Irvine, CA, USA; Trevor stent, Stryker Neurovascular, Mountain View, CA, USA) or an aspiration tubing (Sofia Plus catheter, MicroVention, CA, USA; ACE or Jet 7 catheter, Alameda, CA, USA; React catheter, Medtronic, Irvine, CA, USA), or a combination of both, at the discretion of the neuro interventionist. Rescue therapies including balloon angioplasty and extra-cranial or intra-cranial stenting could be performed in case of LVO caused by atherosclerosis disease. In these cases, antiplatelet agents might be used. The procedure was completed with the use of an Angio-Seal 8F (Terumo) device or manual compression for femoral artery closure.

3. Outcome measurement

The reperfusion result was graded on the final angiogram using the TICI scale. The ICH was confirmed on the NECT or T2* sequence of MRI from 18 to 30 hours after the intervention. The NIHSS was also re-evaluated to determine if it was symptomatic ICH. The functional outcome was assessed by the mRS 90 days post-treatment at a planned visit or via telephone.

4. Statistical analysis

Continuous variables were presented as medians and interquartile ranges (IQR). Categorical variables were presented as frequencies and percentages.

Clinical, imaging, procedural, and outcome variables in two outcome groups were compared using the Mann-Whitney U test for continuous variables and Fisher exact test for categorical variables. Univariate and multivariate logistic regression were used estimate the odds ratio (OR) and the association of prognostic factors with outcomes. P-values ≤ 0.05 were considered statistically significant. Data were processed and analyzed using SPSS software (version 16.0; IBM SPSS Inc, Chicago, USA). Subgroup analyses were done using Stata 16.0 (StataCorp, College Station, Texas, USA).

III. RESULTS

1. Sample characteristics

From December 2020 to September 2022, one hundred twenty consecutive patients presenting AC-LVO within 4.5 hours treated with MT were enrolled in this study.

There were 70 males (58.3%) and 50 females (41.7%). The median age was 66 years (IQR, 59-75). The median baseline NIHSS was 12 (IQR: 10-15).

Of the 120 patients, 39 (32.5%) had occlusions in the ICA, 61 (50.8%) in the M1, and 20 (16.7%) in the M2. The median baseline ASPECTS was 8 (IQR: 7 to 8).

MT was feasible in 118 cases (98.3%). General anesthesia was used in the majority of procedures (112/120 cases, 93.3%). The median time from stroke onset to groin puncture was 211.5 minutes (IQR: 174.3-270.0). The median procedure time from groin puncture to reperfusion was 35.0 minutes (IQR: 25.0-60.0). The median number of passages was 1 (IQR, 1-2), and first-pass recanalization was achieved in 64/120 cases (53.3%). Rescue techniques were needed in 22/120 cases (19.3%).

Overall, successful reperfusion (TICI 2b-3) was achieved in 102/120 cases (85.0%). Perforation/dissection complications occurred in 6/120 cases (5.0%). At follow-up after the treatment, ICH occurred in 45/120 cases (37.5%), of which 7 cases (5.8%) were sICH. Good outcome, defined as having mRS between 0 and 2, was achieved in 70/120 cases (59.3%). The overall mortality rate was 6.7% (8/120 cases).

2. Prognostic factors for Good Outcome (mRS 0-2)

Comparing those who had good outcome to those who did not, there were statistically significant differences in age, baseline NIHSS, initial glucose level, rate of cardioembolism and large-artery atherosclerosis, time from groin puncture to reperfusion, first-pass reperfusion rate, successful reperfusion rate, occurrence of intracranial hemorrhage, and symptomatic intracranial hemorrhage rate (Table 1). In univariate analysis, all of these variables were identified as factors associated with good outcome at 3 months.

Table 1. Two groups based on the good outcome at 90 days

Characteristics of the study cohort (n = 120)	mRS 0-2 (n = 70)	mRS 3-6 (n = 50)	p
Age, year, median (IQR)	65 (58.8-74.0)	70.5 (63.0-77.0)	0.05*
Gender, male, n (%)	42 (60.0)	28 (56.0)	0.66
Baseline NIHSS, median (IQR)	12 (10-14)	14 (10-18)	0.01*
Initial glucose level (mmol/L)	7.4 ± 2.5	8.7 ± 3.8	0.01*
ICA occlusion, n (%)	21 (30.0)	18 (36.0)	0.49
M1 occlusion, n (%)	40 (57.1)	21 (42.0)	0.10
M2 occlusion, n (%)	9 (12.9)	11 (22.0)	0.19
Cardioembolism, n (%)	40 (57.1)	14 (28.0)	< 0.01*
Large-artery atherosclerosis, n (%)	24 (34.3)	33 (66.0)	< 0.01*
Baseline ASPECTS, median (IQR)	7 (7-8)	7 (7-8)	0.07
Pretreatment with alteplase, n (%)	34 (48.6)	26 (52.0)	0.71
General anesthesia, n (%)	64 (91.4)	48 (96.0)	0.32
From onset to admission (minutes)	135.8 ± 59.2	140.1 ± 58.6	0.70
From admission to start of alteplase (minutes)	36.4 ± 23.9	32.2 ± 18.7	0.46

From groin puncture to reperfusion (minutes)	38.9 ± 28.4	58.7 ± 36.5	0.01*
First-pass aspiration, n (%)	12 (17.1)	9 (18.0)	0.90
First-pass stent retriever, n (%)	7 (10.0)	7 (14.0)	0.50
First-pass Solumbra technique, n (%)	50 (71.4)	31 (62.0)	0.28
Number of passages, median (IQR)	1 (1-2)	1 (1-2)	0.47
First-pass reperfusion, n (%)	45 (64.3)	19 (38.0)	0.01*
Rescue therapy, n (%)	9 (12.9)	13 (26.0)	0.08
Successful reperfusion (TICI 2b-3), n (%)	69 (98.6)	33 (66.0)	< 0.01*
Perforation/dissection complication, n (%)	2 (2.9%)	4 (8.0)	0.20
Any intracranial hemorrhage, n (%)	19 (27.1)	26 (52.0)	0.01*
Symptomatic intracranial hemorrhage, n (%)	1 (1.4%)	6 (12.0)	0.02*

IQR: interquartile range, **P* value ≤ 0.05

In multivariate analysis, only initial blood glucose level (OR, 0.86; 95% CI, 0.85-0.87; *p*=0.046), successful recanalization (OR 1.40; 95%CI 1.24-1.58; *p*<0.01), and any intracranial hemorrhage (OR, 0.83; 95% CI, 0.76-0.90; *p*=0.02) were identified as independent prognostic factors of a good outcome at 3 months (Table 2). Patients with hemorrhagic transformation had good outcome less frequently (42.2% versus 68.0%, *p*=0.01) compared to those without it. When dichotomized, patients with initial blood glucose levels ≤ 10 mmol/L (63.4% versus 47.4%; OR, 0.52; 95% CI, 0.24-1.13; *p*=0.07) had a more frequent good outcome.

Table 2. Logistic regression analysis of factors associated with good outcome at 90 days

	Unadjusted OR	95% CI	P	Adjusted OR	95% CI	P	VIF
Age, per 1-year increase	2.05	1.08-3.64	0.04	0.97	0.02-1.35	0.25	-
Baseline NIHSS score, per 1-point increase	2.24	0.73-9.50	0.00	0.85	0.08-4.48	0.057	-
Initial glucose level, per 1-mmol/L increase	1.41	0.56-6.40	0.01	0.86	0.85-0.87	0.046	1.09
Cardioembolism	1.23	0.40-9.64	0.00	0.16	0.98-3.41	0.14	-
Large-artery atherosclerosis	1.00	0.28-12.29	0.00	-	-	-	-
Time from groin puncture to reperfusion, a 1-minute increase	1.27	0.36-3.98	0.04	1.0	0.01-1.81	0.18	-

Successful reperfusion (mTICI 2b-3)	0.74	0.21-12.15	0.00	1.40	1.24-1.58	<0.01	1.43
First-pass reperfusion	0.86	0.27-9.93	0.00	-	-	-	-
Any intracranial hemorrhage	1.07	0.39-7.48	0.01	0.83	0.76-0.90	0.02	1.20
Symptomatic ICH	2.24	1.10-4.17	0.04	-	-	-	-

OR: odds ratio; CI: confidence interval; VIF: variance inflation factors

IV. DISCUSSION

Our study aimed to identify prognostic factors for good clinical outcomes in patients with acute ischemic stroke due to anterior large vessel occlusion who were treated with MT within 4.5 hours from the onset. Successful revascularization status, and the absence of both high initial blood glucose level (>10 mmol/L) and hemorrhagic transformation were independent prognostic factors for good outcomes at 90 days.

The high revascularization efficiency of 85% in our study was consistent with the values reported in previous studies that involved the use of MT within 4.5 hours of onset.[6] Our rate of good clinical outcome of 58.3% at 90 days was also similar to results of other studies, suggesting that recanalization can affect clinical outcome.[5] In our study, successful revascularization (defined as modified TICI ≥ 2b) is a factor (OR, 1.40; 95% CI 1.24-1.58; p < 0,01) associated with good clinical outcomes after MT in patients with AIS due to AC-LVO, which was consistent with two previous studies that also reported successful revascularization as one of the independent factors related to good outcomes.[9-11] Ozdemir et al and Yoon et al both found that successful revascularization was the most powerful independent factors related to good outcome.[11,10]

Intracranial hemorrhagic transformation was the most dangerous complication after MT in acute ischemic stroke. The absence of intracranial hemorrhage was demonstrated as one of the independent factors associated with good outcome in our study (OR, 0.83; 95% CI 0.76-0.90; p=0.02). Patients with hemorrhagic transformation were significantly less likely to have good outcomes (42.2% versus 68.0%) compared to those without it. This finding was consistent with the report of Yoon et al, which included 335 patients with anterior circulation stroke who received MT with stent retriever.[11] In that study, parenchymal hemorrhage occurred in 8.9% of the patients and was associated with a lower likelihood of good outcomes (OR, 0.15; 95% CI, 0.05-0.46, p<0.01).[11]

Our analysis also revealed the association between initial blood glucose level and good clinical outcomes. The findings observed in our study mirror those of the previous studies that examined the effect of high blood glucose levels on poor clinical outcomes.[8,10] Ozdemir et al. reported a 1.43-fold decrease in the probability of a good outcome for each 1.1 mmol/L increase in blood glucose at admission. There are several explanations regarding the contribution of higher glucose levels to poor outcomes. Hyperglycemia is associated with larger infarct volumes and reduced salvage parenchyma.[10] Additionally, high glucose level at admission was associated with increased risk of symptomatic intracranial hemorrhage after mechanical thrombectomy.[10]

Our study has two main limitations. The first is the restricted number of cases at our institution, which might overestimate the differences in the outcomes. Finally, thrombus length measured on imaging, collateral status, as well as the role of advanced MRI for detecting chronic hemorrhage, which may affect the efficacy of IVT before MT, was not evaluated in our study.

V. CONCLUSIONS

The present study found that successful revascularization, the absence of both high initial blood glucose level (>10 mmol/L), and hemorrhagic transformation post-treatment were significant factors associated with good outcome in patients undergoing MT within 4.5 hours from the onset.

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