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Mechanical Thrombectomy Outcome Predictors in Stroke Patients with M2 Occlusion: A Single-Center Retrospective Study

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■ BACKGROUND: **Mechanical thrombectomy (MT) has demonstrated benefit in patients with acute ischemic stroke due to proximal large-vessel occlusion. However, it is unclear whether these results can be extrapolated to patients with an occlusion of the second segment (M2) of the middle cerebral artery (MCA). We sought to study outcomes in patients with M2 occlusion treated with MT and to better understand clinical predictors of these outcomes.**

■ METHODS: **We performed a single-center retrospective analysis of consecutive patients with acute MCA M2 segment occlusion who underwent stent retriever MT. We correlated clinical and radiographic outcomes with demographic, clinical, and technical characteristics.**

■ RESULTS: **Thirty-seven patients were included in the analysis (median admission National Institutes of Health Stroke Scale [NIHSS] score, 15 [12–19], mean age 74 [67–80] years, 48.6% women). Good clinical outcome at 3 months (modified Rankin Scale ≤2) was achieved in 48.6% of patients. Baseline NIHSS was a predictor of clinical outcomes, based on modified Rankin Scale distribution at 3 months after MT ($P = 0.015$, odds ratio 1.63, 95% confidence interval 1.01–2.43).**

■ CONCLUSIONS: **The results of our single-institution experience suggest that MT-based endovascular therapy for M2 occlusions is safe and effective. Baseline NIHSS was a predictor of outcomes in patients treated with MT for M2 segment occlusion of the MCA.**

INTRODUCTION

The site of arterial occlusion represents one of the most important factors determining outcome after anterior circulation ischemic stroke.[1,2] According to 5 published randomized controlled trials, mechanical thrombectomy (MT) is beneficial for patients with acute proximal (i.e., internal carotid artery [ICA] terminus and M1 segment of the middle cerebral artery [MCA]), anterior circulation, and intracranial arterial occlusions.[3-7] It is unclear, however, whether these results can be extrapolated to patients with an occlusion of the second segment of the MCA (M2 occlusion). As the result of the distal location, smaller diameter, and thinner walls of M2 segment of the MCA, its MT is technically more challenging and may be associated with a greater risk of periprocedural complications. Moreover, scarce data are available on the safety and outcomes of patients with distal MCA occlusion treated with MT.[8,9] In this single-center retrospective study, we analyzed clinical outcome post-MT in patients with acute ischemic stroke from isolated occlusions in M2 segment of the MCA to identify patient groups that were more likely to benefit from the stent retriever MT.

Key words
- Middle cerebral artery
- Stroke
- Thrombectomy

Abbreviations and Acronyms

CTP: Computed tomography perfusion
ICA: Internal carotid artery
ICH: Intracranial hemorrhage
IV: Intravenous
MCA: Middle cerebral artery
mRS: Modified Rankin Scale
MT: Mechanical thrombectomy
NCCT: Non–contrast-enhanced computed tomography
NIHSS: National Institutes of Health Stroke Scale
PH: Parenchymal hematoma
TICI: Thrombolysis in cerebral infarction

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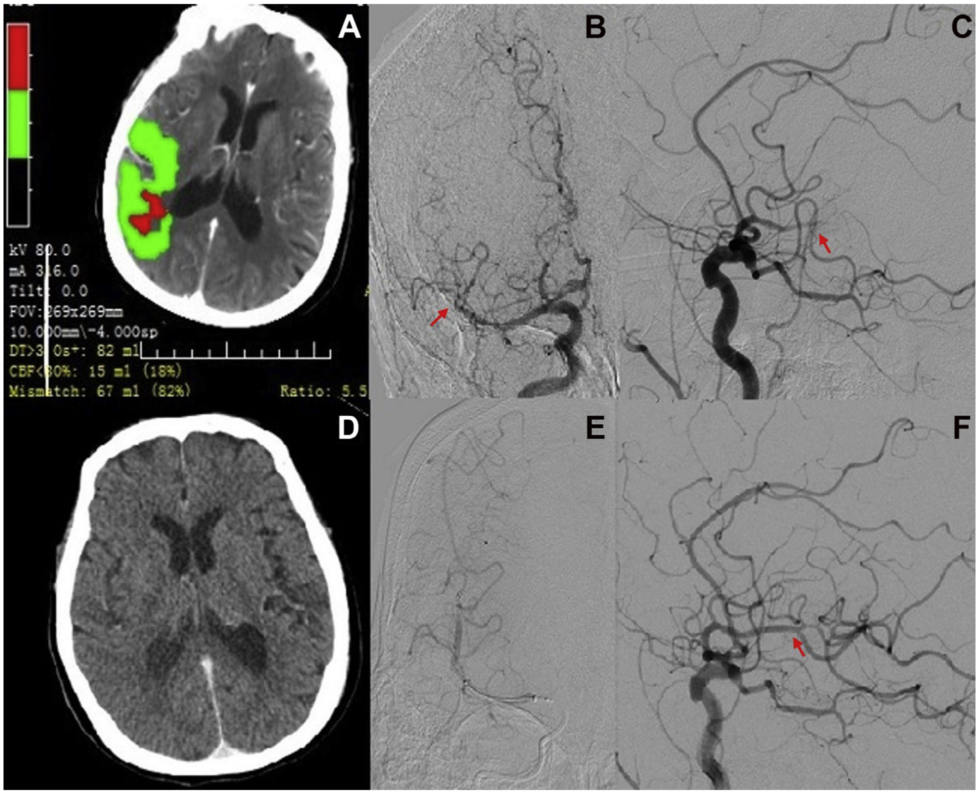

Figure 1. The patient with a good outcome with M2 cerebral artery occlusion. (**A**) Computed tomography (CT) perfusion revealed that the mismatch between penumbra and core infarct was greater than 1.8. (**B**) Anteroposterior view before treatment showed M2 occlusion of cerebral artery (*red arrow*). (**C**) Lateral view before treatment showed M2 occlusion of cerebral artery (*red arrow*). (**E**) A retrievable stent (Solitaire FR 4 *20 mm) is deployed across the occlusion in the M2 segment. (**F**) Anteroposterior view of a digital subtraction angiogram demonstrated Thrombolysis in Cerebral Infarction grade 3 reperfusion (*red arrow*). (**D**) Review of CT of the head showed no bleeding after thrombectomy.

METHODS

Study Design, Setting, and Participants

The single-center retrospective study was approved by the local institutional review board for retrospective data collection and review. Data were collected on consecutive stroke cases with occlusion in the M2 segment of the MCA that were treated with MT between February 2016 and August 2018. The center selected the patients with occlusion in the M2 segment of the MCA within 24 hours of the stroke onset. The M2 segment is defined as the MCA segment with vertical MCA branches in the sylvian fissure originating at the genu and extending to the next genu at the level of the operculum.[10] Cases with combined occlusions of M1 and M2 segments and isolated tandem occlusion at a more proximal location (cervical ICA or terminal ICA) were excluded from the analysis.

Intravenous (IV) thrombolysis was not selected as an exclusion criterion. When patients presented with stroke within 24 hours of onset, pre-stroke modified Rankin Scale (mRS) score ≤1 point, age ≥18 years, National Institutes of Health Stroke Scale (NIHSS) ≥6 points, Alberta Stroke Program Early CT Score ≥6 points, considering large-vessel occlusion, multimode computed tomography was used to confirm large-vessel occlusion amenable to intra-arterial therapy while evaluating potential candidates for MT. The imaging evaluation consisted of non−contrast-enhanced computed tomography (NCCT), computed tomography angiography, and computed tomography perfusion (CTP). The selection of patients as candidates for MT was based on the absence of hemorrhage and extensive irreversible ischemic changes in NCCT and evaluation of the amount of salvageable tissue in CTP imaging such that the mismatch between the penumbra and the core infarct was greater than 1.8. Stroke cases with ischemic core comprising more than one third of the MCA territory were excluded from the mechanical treatment.

Data Collection

Baseline demographics (age, sex, smoking status, history of stroke or transient ischemic attack, hypertension, diabetes, coronary heart disease, atrial fibrillation, hyperlipidemia, and levels of glycohemoglobin and homocysteine) were collected from the patient records. Information regarding baseline NIHSS score at the time of presentation, IV tissue plasminogen activator use in the emergency department, treatment time (symptom onset to

Table 1. Patient Characteristics

	Overall (*n* = 37)	Good Outcome (mRS ≤2, *n* = 18)	Poor Outcome (mRS >2, *n* = 19)	*P* Value
Patient characteristics				
Age, median (IQR)	74.0 (67.0—80.0)	69.0 (56.3—77.0)	78.0 (71.0—82.0)	0.018*
Sex (female), % (*n*)	48.6% (18/37)	66.7% (12/18)	31.6% (6/19)	0.050
Baseline NIHSS, median (IQR)	15.0 (12.0—19.0)	13.5 (11.8—17.3)	19.0 (13.0—21.0)	0.029*
ASPECTS, median (IQR)	10 (8—10)	10 (8—10)	10 (8—10)	1.000
History of stroke or TIA, % (*n*)	8.1% (3/37)	5.6% (1/18)	10.5% (2/19)	1.000
Hypertension, % (*n*)	70.3% (26/37)	61.1% (11/18)	78.9% (15/19)	0.295
Diabetes, % (*n*)	18.9% (7/37)	22.2% (4/18)	15.8% (3/19)	0.693
Hyperlipidemia, % (*n*)	16.2% (6/37)	5.6% (1/18)	26.3% (5/19)	0.180
Coronary artery disease, % (*n*)	24.3% (9/37)	16.7% (3/18)	31.6% (6/19)	0.447
Atrial fibrillation, % (*n*)	67.6% (25/37)	77.8% (14/18)	57.9% (11/19)	0.295
Smoker, % (*n*)	16.2% (6/37)	16.7% (3/18)	15.8% (3/19)	1.000
Admission SBP, mm Hg, median (IQR)	159.0 (125.0—178.5)	155.5 (127.0—167.0)	168.0 (120.0—190.0)	0.162
Admission DBP, mm Hg, median (IQR)	83.0 (76.0—94.0)	83.0 (80.5—90.3)	89.0 (70.0—94.0)	0.808
Admission serum glucose, mg/dL, median (IQR)	7.7 (6.5—8.8)	7.4 (6.5—8.3)	7.9 (6.5—8.9)	0.531
Admission LDL, mmol/L, median (IQR)	2.0 (1.4–2.3)	2.1 (1.5–2.4)	1.6 (1.2–2.1)	0.125
Admission glycohemoglobin, mmol/L, median (IQR)	5.6 (5.3—6.3)	5.6 (5.3—6.3)	5.6 (5.3—6.3)	0.947
Admission homocysteine, mmol/L, median (IQR)	14.0 (10.0—22.3)	14.0 (10.0—22.0)	14.0 (10.5—22.5)	1.000
Fasting blood glucose following MT, mmol/L, median (IQR)	7.3 (5.8—8.2)	6.5 (4.6—7.9)	8.0 (6.4—9.3)	0.020*
Occlusion site				
Left hemisphere, % (*n*)	54.1% (20/37)	55.6% (10/18)	52.6% (10/19)	1.000
Right hemisphere, % (*n*)	45.9% (17/37)	44.4% (8/18)	47.4% (9/19)	1.000
Treatment details				
IV tPA administration, % (*n*)	35.1% (13/37)	33.3% (6/18)	36.8% (7/19)	1.000
Symptom onset to femoral arterial puncture (minutes), median (IQR)	287.0 (210.0—347.5)	297.0 (210.0—342.5)	287.0 (202.0—360.0)	0.715
Duration of procedure, minutes, median (IQR)	46.0 (40.0—76.0)	44.0 (41.5—56.3)	61.0 (40.0—95.0)	0.166
Onset to recanalization, minutes, median (IQR)	338.0 (255.0—413.5)	321.0 (256.8—385.0)	338.0 (250.0—430.0)	0.738
Number of pass, median (IQR)	2.0 (1.0—3.0)	1.0 (1.0—2.0)	2.0 (1.0—3.0)	0.077
Time from symptom onset to femoral arterial puncture >360, % (*n*)	21.6% (8/37)	22.2% (4/18)	21.1% (4/19)	1.000

mRS, modified Rankin score; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; TIA, transient ischemic attack; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; IV tPA, intravenous tissue plasminogen activator.
*$P < 0.05$; *P* value is calculated by the Fisher exact test for binary variables and by Mann—Whitney *U* test for continuous data.

femoral arterial puncture, duration of procedure, onset to recanalization), thrombolysis in cerebral infarction (TICI) grading, and possible complications was stored in a devised questionnaire. Fasting blood glucose levels were recorded within the first 12 hours following MT. A follow-up NCCT was performed 24 hours after MT. Revascularization was evaluated with TICI grading, which was scored from the final digital subtraction angiography control runs of the intervention. A good recanalization was defined as a TICI score of ≥2b, whereas an excellent recanalization was defined as a TICI score of 3. The clinical outcome was measured with mRS, evaluated 3 months after the stroke based on a follow-up visit to a neurologist or a telephonic interview by the neurologist, where a good clinical outcome was defined as an mRS score of ≤2. Hemorrhagic complications were classified based on the European Cooperative Acute Stroke Study III (ECASS III)-described criteria.[11]

Recanalization Therapies

MT was performed using a tri-axial system consisting of an 8F guiding catheter and a distal access catheter through which a

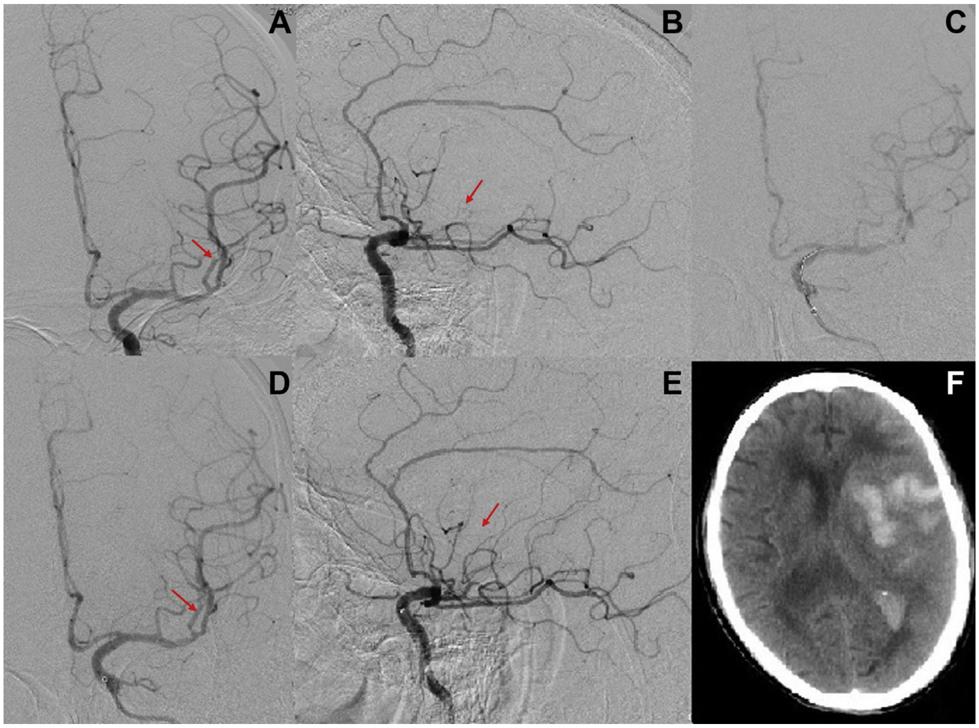

Figure 2. The patient with a poor outcome with M2 cerebral artery occlusion. (**A**) Anteroposterior view before treatment showed M2 occlusion of cerebral artery (*red arrow*). (**B**) Lateral view before treatment showed M2 occlusion of cerebral artery (*red arrow*). (**C**) A retrievable stent (Solitaire FR 4 *20 mm) is deployed across the occlusion in the M2 segment. (**D**) Anteroposterior view of a digital subtraction angiogram demonstrated Thrombolysis in Cerebral Infarction grade 2B reperfusion (*red arrow*). (**E**) Lateral view of a digital subtraction angiogram demonstrated Thrombolysis in Cerebral Infarction grade 2B reperfusion (*red arrow*). (**F**) Review of computed tomography of the head showed parenchymal hematoma type 2 bleeding after thrombectomy.

micro-catheter was inserted with the aid of a 0.014" micro-guidewire. The micro-catheter was navigated through the occluded segment of the artery and a Solitaire stent retriever (Medtronic, Minneapolis, Minnesota, USA) was then positioned through it to the thrombus site. The stent was left in place for 5 minutes, and then at the time of retrieval, the intermediate catheter was aspirated forcefully. The same procedure was repeated until satisfactory circulation was restored. Because there was no balloon catheter in our center, all patients underwent use of the Solitaire stent for MT. Procedures were performed with the patient under conscious sedation.

Statistical Analyses

For patient characteristics and outcomes, differences between groups (mRS $\leq$2 vs. mRS $>$2) were estimated by the Mann—Whitney U test for continuous data and the Fisher exact test for categorical data. Here, we did not perform χ^2 tests for binary data as the result of small sample sizes ($n < 40$). All variables that were associated with primary outcomes on univariate analysis with a P value of less than 0.1 were included in the multivariate analysis. Multivariate logistic regression based on the likelihood ratio (forward selection method) was then used to assess independent predictors of primary outcomes. Statistical analyses were performed using IBM SPSS statistics, version 21 (IBM Corp., Armonk, New York, USA). For all statistical analyses, all P values were based on 2-tailed tests and $P < 0.05$ was considered statistically significant.

RESULTS

A total of 37 patients with acute ischemic stroke due to occlusion in M2 segment of the MCA were selected for the final analysis. Good outcome was found in 18 cases and poor outcome in 19 cases (**Figure 1**). There were no important differences in medical histories between the 2 groups. The median age was 74.0 (67.0—80.0) years, 48.6% of the patients were women, and the median NIHSS score at the time of admission was 15. M2 occlusions occurred on the left side in 20 patients (54.1%). Thirteen patients (35.1%) received IV tissue plasminogen activator before the procedure. Mean time from symptom onset to groin puncture, duration of procedure, and symptom onset to recanalization were 287.0 (210.0—347.5) minutes, 46.0 (40.0—76.0) minutes, and 338.0 (255.0—413.5) minutes. The number of passes in good-outcome group was less than the poor-outcome group, 1.0 (1.0—2.0) and 2.0 (1.0—3.0) respectively. The 2

Table 2. Outcomes After Mechanical Thrombectomy in M2 Segment of Middle Cerebral Artery Stroke Patients

	Overall (n = 37)	Good Outcome (mRS ≤2, n = 18)	Poor Outcome (mRS >2, n = 19)	P Value
TICI score, % (n)				0.357
TICI 1	2.7% (1/37)	5.6% (1/18)	0% (0/19)	
TICI 2a	2.7% (1/37)	0% (0/18)	5.3% (1/19)	
TICI 2b	18.9% (7/37)	11.1% (2/18)	26.3% (5/19)	
TICI 3	75.7% (28/37)	83.3% (15/18)	68.4% (13/19)	
Hemorrhagic complication, % (n)				
Any ICH	40.5% (15/37)	16.7 (3/18)	63.2 (12/19)	0.007*
Bleeding classification, % (n)				
HI1	5.4% (2/37)	0% (0/18)	10.5% (2/19)	0.486
HI2	18.9% (7/37)	16.7% (3/18)	21.1% (4/19)	1.000
PH1	5.4% (2/37)	0% (0/18)	10.5% (2/19)	0.486
PH2	10.8% (4/37)	0% (0/18)	21.1% (4/19)	0.105
PH1 + PH2	16.2% (6/37)	0% (0/18)	31.6% (6/19)	0.020*
sICH	10.8% (4/37)	0% (0/18)	21.1% (4/19)	0.105

mRS, modified Rankin score; TICI, Thrombolysis In Cerebral Infarction; ICH, intracranial hemorrhage; HI, hemorrhagic infarction; PH, parenchymal hematoma; sICH, symptomatic intracranial hemorrhage.
*$P < 0$ .05; P value is calculated by the Fisher exact test for binary variables and by the Mann—Whitney U test for continuous data.

groups were not statistically significant. Baseline clinical and imaging characteristics of the 37 patients are shown in Table 1.

Symptomatic intracranial hemorrhage (ICH) occurred in 4 patients (10.8%), 2 of whom had been treated with IV tissue plasminogen activator (Figure 2). After 3 months, 48.6% of patients had a good outcome and the death rate was 13.5%. Age and baseline NIHSS score were greater in patients with poor outcome in comparison with patients with good outcome (78.0 vs. 69.0, P = 0.018 and 19.0 vs. 13.5, P = 0.0029, respectively). ICH (63.2% vs. 16.7%, P = 0.007), parenchymal hematoma (PH) (31.6% vs. 0.0%, P = 0.020) (Table 2), and hyperglycemia following MT (8.0 vs. 6.5, P = 0.020) were associated with poor clinical outcome.

The distribution of vascular risk factors was similar between the 2 groups (Table 1). In 8 of 37 cases (21.6%), MT was initiated after 6 hours of symptom onset. Clinical outcomes were similar between patients who were treated within the first 6 hours in comparison with patients treated beyond the 6-hour window (rate of favorable clinical outcome was 50.0% vs. 50.0%, P = 1.000). Successful recanalization was achieved in 35 (94.6%) cases, of which 28 (75.7%) cases showed excellent recanalization. In multivariate logistic regression analysis (Table 3), baseline NIHSS score was found to be predictive of poor outcome (poor vs. good, P = 0.0015, odds ratio 1.63, 95% confidence interval 1.01—2.43).

DISCUSSION

Occlusions of the M2 segment of the MCA may cause significant clinical effects, particularly when they occur in the dominant cerebral hemisphere; however, MT of such occlusions remains controversial. The prognosis and best management practices for acute distal intracranial arterial occlusions, including M2 MCA, are not clear. Few studies have previously examined the mechanical treatment of patients with an M2 occlusion. In this single-center retrospective study of patients who underwent MT with stent retrievers for isolated acute M2 occlusions with moderate-to-severe stroke severities, 48.6% of patients achieved a good clinical outcome after 3 months with a low mortality rate. Similar clinical outcomes have been shown by multiple other studies.[12-14]

However, the good outcome rate was lower than some studies. In a retrospective summary from Sarraj et al.,[15] patients with endovascular treatment who achieved good clinical outcomes after 90 days was as high as 62.8%, perhaps because our cohort was older (74.0 vs. 68.0). Coutinho et al.[10] analyzed M2 occlusion in the Solitaire Flow Restoration Thrombectomy for Acute Revascularization (STAR), SOLITAIRE FR With the Intention For Thrombectomy (SWIFT), and Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) studies, with a good outcome of 60% at 3 months, possibly associated with lower

Table 3. Multivariate Logistic Regression for Predictors of Bad Outcomes (mRS 3—6)

	OR	95% CI	P Value
Baseline NIHSS	1.63	1.01—2.43	0.015*

mRs, modified Rankin scale; NIHSS, OR, odds ratio; CI, confidence interval; National Institutes of Health Stroke Scale.
*$P < 0.05$.

NIHSS scores (13.0 vs. 15) and shorter duration of procedure (29.0 vs. 46.0) in his group.

In the study by Sarraj et al.,[15] the best medical management group, only 35.4% of patients achieved a good clinical outcome after 3 months. Rahme et al.[16] analyzed the M2 occlusion subgroup of the Prolyse in Acute Cerebral Thromboembolism II (PROACT-II) trial and found that the best medical management team only achieved a good outcome of 28.6%. The high rates of successful recanalization (94.6%), good clinical outcomes (48.6%), and low mortality (13.5%) further support the role of MT in patients presenting with symptomatic acute M2 segment occlusions.

Although the good clinical outcome after 3 months for our study was similar to that of previous studies, the hemorrhagic conversion rate and symptomatic ICH rate were greater.[12,13] This may be attributed to the use of stent retriever thrombectomy in 37 patients instead of using distal aspiration alone. However, similar to a meta-analysis by Saber et al.,[17] mortality and symptomatic ICH rates were 16% and 10%. The results of the DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo) and the DEFUSE 3 (The Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) trials suggested that MT may be beneficial up to 24 hours after the stroke onset in carefully selected patients.[18,19] However, the DAWN and the DEFUSE 3 trials chose the patients with proximal MCA or ICA occlusions. In this study of M2 occlusions, 21.6% patients were treated with MT, which was initiated beyond the first 6-hour window of symptom onset, and the clinical outcomes were similar irrespective of time to treatment. All patients in our cohort were selected for MT using CTP imaging; therefore, under the guidance of CTP imaging, MT for M2 occlusion treatment may be feasible when initiated beyond the first 6-hour window of symptom onset.

In this study of treatment of M2 occlusions, advanced age, ICH, PH1 + PH2, and hyperglycemia following thrombectomy were found to be predictive of poor outcomes. Hyperglycemia causes neurons to become stunned with the subsequent arrest of protein synthesis and mitochondrial activity. This arrest can lead to cell death following ischemia. If patients have hyperglycemia following thrombectomy, they are likely to have a poor outcome.[20] The baseline NIHSS score was found to be an independent predictor of poor outcomes, similar to the findings of previous trials of proximal occlusions. Thus, stroke severity was shown to serve as a powerful predictor of clinical outcome in patients treated with MT.[21,22] However, the time from onset of symptoms to recanalization was not predictive of poor outcomes, unlike the findings of previous trials of proximal occlusions.[22,23] Overall, our findings share similarities with outcomes in patients who are treated with thrombectomy for more proximal anterior circulation strokes, suggesting that MT might be effective for M2 occlusion.

Our study had several limitations, including the retrospective design, small sample size, lack of independent core laboratory evaluation, and variations in patient selection. There may be an inherent selection bias of treating patients with M2 occlusions with only severe initial presentations, left hemispheric syndromes, or favorable anatomy. Furthermore, we did not compare our cohort of patients with M2 occlusions with patients who were treated conservatively. Lastly, the type of endovascular treatment was such that all patients were treated only with stent retriever MT without direct distal aspiration. Further randomized multicenter clinical trials are needed to definitively prove the benefit of MT for patients with more distal MCA occlusion and to clarify which patients with M2 occlusion may benefit from MT. To the best of our knowledge, there is a trial ongoing in Europe involving distal vascular MT (Contact Aspiration vs. Stent Retriever for Successful Revascularization 2 [ASTER2], NCT03290885); we hope that the data from this trial provides better management protocols for these patients.

CONCLUSIONS

This single-center retrospective study demonstrated safety and efficacy of MT in patients with M2 occlusion. Baseline NIHSS score was found to be predictive of clinical outcome with MT. We suggest that under the guidance of CTP imaging, MT for M2 occlusions may be feasible when initiated beyond the first 6-hour window of symptom onset.

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