Online November 29, 2022
Journal of Neuroendovascular Therapy 2023; 17: 15–21
DOI: 10.5797/jnet.oa.2022-0057

Original Article

Complete Recanalization in Mechanical Thrombectomy Is Associated with Favorable Functional Outcome for M2 Occlusions

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Objective: There are insufficient coherent reports on mechanical thrombectomy (MT) for occlusion of the second segment of the middle cerebral artery (M2 occlusion) in a real-world clinical setting. We evaluated the efficacy and safety of MT for M2 occlusions and compared the primary thrombectomy strategies (stent retriever, aspiration catheter, and combined technique) to analyze factors predicting good functional outcomes.
Methods: We evaluated background factors, preprocedural factors, procedural factors, and procedural time for patients who underwent MT for M2 occlusions from our retrospective cohort. According to the modified Rankin Scale (mRS) score three months after MT, patients were divided into good (mRS ≤2) and poor (mRS ≥3) prognosis groups.
Results: A total of 29 patients (median age, 78 years; 11 [37.9%] females) were included in the study. In this cohort, rates of successful reperfusion, thrombolysis in cerebral infarction (TICI) 3, postprocedural hemorrhage (PPH), and symptomatic PPH were 82.8, 34.5, 31.0, and 0%, respectively. Good prognoses were achieved in 13 (45%) cases. A prognostic factor of MT for M2 occlusions is TICI 3 from multivariate analysis (OR, 11.7; 95% CI, 1.003–136; p = 0.0497). There was no statistically significant difference in the functional outcome three months after MT based on the choice of the primary thrombectomy strategy.
Conclusion: MT for M2 occlusions is a reliable and relatively safe procedure. The presence of TICI 3 was a prognostic factor in this cohort. Future studies are warranted to investigate the optimal thrombectomy strategy for medium vessel occlusion.

Keywords ▶ M2 occlusion, mechanical thrombectomy, prognostic factors, TICI 3

Introduction

Since 2015, several randomized clinical trials have established the efficacy and safety of mechanical thrombectomy (MT) for large vessel occlusion (LVO) in the anterior circulation.[1)] MT is now ranked as a standard therapy,[2–4)] and its indication is expanding to large ischemic core,[5,6)] posterior circulation ischemic stroke,[7)] and acute ischemic stroke with extended time windows.[8,9)] Under such circumstances, the indication of MT for medium vessel occlusion (MeVO) is also discussed, and several studies have indicated that MT for the second segment of the middle cerebral artery (MCA M2) occlusion is safe and effective in improving patients' functional outcomes with a lower rate of adverse events.[10)] However, studies reporting the MT outcome for M2 occlusions in real-world clinical settings remain insufficient, and prognostic factors predicting good outcomes after the procedure are not well discussed. Meanwhile, several studies have compared the different MT strategies such as aspiration catheter (AC), stent retriever (SR), and combined technique and the optimal strategy for each in LVO.[11–13)] However, few studies have analyzed MT strategies for M2 occlusions.[10)]

Therefore, this retrospective study aimed to evaluate the efficacy and safety of MT for M2 occlusion and analyze the

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prognostic factors for MT. We also compared first-line treatment strategy outcomes to identify which primary strategy exhibited the best outcome.

Materials and Methods

Patient population

We retrospectively analyzed the data of patients who underwent MT for M2 occlusions at our institution between January 2016 and March 2020.

We defined M2 as the middle cerebral artery (MCA) extending from the genu to the top of the Sylvian fissure and the circular sulcus.[14] The following procedural indications were considered for M2 occlusion: no age limit, within 6 hours from onset, National Institutes of Health Stroke Scale (NIHSS) ≥6, and diffusion-weighted image (DWI)-Alberta stroke program early CT score (ASPECTS) ≥6.[2] All patients in this cohort received MRI scans prior to the procedures. Indication for each patient was carefully considered, and for the cases having penumbra area in relation to the occluded M2 and the complete ischemic area on DWI, the procedure was performed even beyond 6 hours of symptom onset.[15]

Patients with tandem lesions, pre-stroke modified Rankin Scale (mRS) score 3–5, transferred from other hospitals, and in-hospital onset were excluded. Based on the mRS score at 3 months after MT, patients were divided into good (mRS ≤2) and poor (mRS ≥3) prognosis groups. Besides procedural factors and time, patient's background factors and preprocedural factors were compared between the groups.

Endovascular procedure

All interventional procedures were performed using a biplane angiography system (Artis Q biplane; Siemens Healthineers, Erlangen, Germany) and supervised by the board-certified neurointerventional specialists (SK and OI). Transfemoral cerebral angiography was performed under local anesthesia. The MT procedure was initiated after assessing the vascular architecture of the occluded artery and collateral vessel status. A 9 F balloon-tipped guide catheter (BGC Optimo; Tokai Medical, Aichi, Japan) was advanced to the cervical internal carotid artery. The patients were divided into three groups based on endovascular therapy (EVT) technique used: AC, SR, and combined technique. In the AC group, we performed a direct aspiration first-pass technique using a perfusion catheter (ACE60 or 4MAX; Penumbra, Alameda, CA, USA).[16] For the SR group, the procedures were performed using Trevo (Trevo XP ProVue 3 × 40 mm; Stryker, Kalamazoo, MI, USA) or Solitaire (Solitaire FR 4 × 20 mm or Solitaire Platinum 4 × 40 mm; Medtronic, CA, USA). In the combined technique group, we performed continuous aspiration before the intracranial vascular embolectomy using a reperfusion catheter (ACE60 or 4MAX) and SR (Trevo XP ProVue 3 × 40 mm, Solitaire FR 4 × 20 mm, or Solitaire Platinum 4 × 40 mm).[17] The case in which the AC was not guided to the occluded site and used as a distal access catheter (DAC) was classified as the combined technique group. Throughout the study period, the combined technique was our primary strategy; however, AC or SR was used if the distal lesion was easily accessible. The first two MT procedures for a given case were attempted with the same EVT technique; however, if no successful reperfusion was achieved, a different EVT technique was employed. The procedure was terminated when thrombolysis in cerebral infarction (TICI) 2b or better was obtained. Even if the successful reperfusion over TICI 2b was not accomplished, the procedure was abandoned when the procedure time extended beyond approximately 60 minutes. Intravenous infusion of tissue plasminogen activator (tPA) was performed in all patients without contraindications.

Clinical, radiological, and angiographical data collection

Clinical characteristics, medical history, and angiographic findings were collected from the patient records. NIHSS scores were assessed at baseline, whereas ASPECTS was calculated from the initial DWI. The TICI score was assessed at the time of the final angiography after thrombectomy by the physicians not directly involved in that procedures (SK or YS). Successful reperfusion was defined as a TICI score of 2B or 3. Control CT scans were obtained immediately after EVT and 24 hours after the procedure to check for postprocedural hemorrhage (PPH). Symptomatic PPH was defined as any hemorrhage with a ≥4-point increase in the NIHSS score within 24 hours.

Statistical analysis

All statistical analyses were performed using R software (version 4.1.1; R Core Team). Numerical variables were expressed as median (interquartile range) and compared using the Mann–Whitney U test. Categorical data were expressed as counts and percentages and compared using the Fisher's exact test or the chi-square test. All reported p values were two-sided, and values <0.05 were considered significant. Univariate and multivariate analyses were performed using logistic regression models. In

Table 1 Patient characteristics

	All (29)	Good group (13)	Poor group (16)	*p* value
Patient background				
Age	78 (73–84)	77 (72–80)	82 (73–85)	0.12
Female	11 (37.9%)	2 (15.4%)	9 (56.3%)	0.052
Af	17 (58.6%)	8 (61.5%)	9 (56.3%)	0.77
HTN	23 (79.3%)	9 (69.2%)	14 (87.5%)	0.23
DM	3 (10.3%)	0 (0%)	3 (18.8%)	0.23
DL	9 (31.0%)	3 (23.1%)	6 (33.3%)	0.40
Antiplatelet drugs	3 (10.3%)	1 (7.7%)	2 (12.5%)	0.67
Anticoagulant drugs	10 (34.5%)	5 (38.5%)	5 (31.3%)	0.68
Statin	5 (17.2%)	2 (15.4%)	3 (18.8%)	0.81
Preprocedural factors				
Baseline NIHSS	15 (9–20)	14 (11–17)	17 (13–20)	0.21
Baseline ASPECTS	7 (6–8)	7 (6–8)	7 (6–7)	0.75
tPA	17 (58.6%)	9 (69.2%)	8 (50.0%)	0.30
Left	17 (58.6%)	8 (61.5%)	9 (56.3%)	0.77
Dominant M2	20 (69.0%)	8 (61.5%)	12 (66.7%)	0.44
Upward M1	19 (65.5%)	10 (76.9%)	9 (56.3%)	0.24
Procedural factors				
TICI ≥2b	24 (82.8%)	12 (92.3%)	12 (75.0%)	0.22
TICI 3	10 (34.5%)	8 (61.5%)	2 (12.5%)	0.016
1 pass TICI 3	8 (27.6%)	5 (38.5%)	3 (18.8%)	0.40
PPH	9 (31.0%)	3 (23.1%)	6 (37.5%)	0.40
Symptomatic PPH	0 (0%)	0 (0%)	0 (0%)	1
Combined technique	9 (31.0%)	2 (15.4%)	7 (43.8%)	0.10
AC	6 (20.7%)	4 (30.8%)	2 (12.5%)	0.23
SR	15 (51.7%)	7 (53.8%)	8 (50.0%)	0.84
Number of pass	2 (1–3)	2 (1–3)	2 (1–3)	0.65
Procedural time				
Onset to door	70 (57–204)	67 (45–87)	136.5 (60–282)	0.09987
Door to puncture	35 (31–40)	35 (31–41)	36 (30–39)	0.86
Picture to puncture	54 (39–61)	55 (48–60)	48.5 (37–63)	0.83
Puncture to reperfusion	70 (55–102)	63 (52–70)	90 (57–116)	0.091
O2R	260 (213–387)	213 (198–271)	315 (238–86)	0.004

AC: aspiration catheter; Af: atrial fibrillation; ASPECTS: Alberta Stroke Program Early CT Score; DL: dyslipidemia; DM: diabetes mellitus; HTN: hypertension; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; O2R: onset to reperfusion; PPH: postprocedural hemorrhage; SR: stent retriever; TICI: thrombolysis in cerebral infarction; tPA: tissue plasminogen activator

Table 1, items with $p \leq 0.1$ are used as explanatory variables in univariate analysis, whereas those with $p \leq 0.05$ in univariate analysis are employed as explanatory variables in multivariate analysis. For multiple comparisons, Bonferroni correction is applied.

Ethics

Informed consent was obtained from all the patients. The research within our submission has been approved by the Ethics Institutional Review Board of Showa General Hospital.

Results

During the study period, 210 MTs were performed in our department. Of these, 40 (19%) patients underwent MT for M2 occlusions. Eleven cases were excluded from the current study (one case had tandem lesions, four cases were in hospital onset, two cases were transported from other hospitals, and four cases had preprocedural mRS >2). As a result, this study included 29 patients with M2 occlusion. The patients' characteristics are listed in **Table 1**. The cohort included 11 women with a median age of 78 years (73–84 years). The median onset-to-puncture time was 112 min (90–244 min). Adjuvant tPA was administered in 17 (58.6%) cases. The primary MT strategy was SR in 14 cases, AC in six cases, and combined technique in nine cases.

The rates of successful recanalization, TICI 3 recanalization, PPH, and symptomatic PPH were 82.8, 34.5, 31.0, and 0%, respectively. The median number of passes was 2 (1–3) in the entire study group. Regarding functional

Table 2 Multivariate analysis to identify factors predicting good outcome

	Univariate			Multivariate		
	OR	95% CI	*p* value	OR	95% CI	*p* value
TICI 3	11.2	2.1–93.8	0.0107	11.7	1.003–136	0.0497
Female	0.14	0.02–0.75	0.0333	0.42	0.009–1.27	0.07
O2R	0.99	0.98–0.998	0.0492	0.99	0.98–1.003	0.20
P2R	0.981	0.955–0.999	0.0909			
O2D	0.993	0.983–0.999	0.0957			
Combined	0.23	0.03–1.26	0.11			

CI: confidence interval; combined: combined technique; O2D: onset to door; O2R: onset to reperfusion; OR: odds ratio; P2R: puncture to reperfusion; TICI: thrombolysis in cerebral infarction

Table 3 Procedural outcome for each thrombectomy strategy

	Combined (9)	AC (6)	SR (14)
Good outcome	2 (22.2%)	4 (66.7%)	7 (50.0%)
P2R	71 (45–212)	61 (38–102)	72 (34–218)
Number of pass	3 (2–7)	2 (1–3)	1 (1–4)
TICI ≥2b	7 (77.8%)	5 (83.3%)	12 (85.7%)
TICI 3	1 (11.1%)	3 (50.0%)	6 (42.9%)
PPH	5 (55.6%)	0 (0%)	4 (28.6%)
Symptomatic PPH	0 (0%)	0 (0%)	0 (0%)

AC: aspiration catheter; P2R: puncture to reperfusion; PPH: postprocedural hemorrhage; SR: stent retriever; TICI: thrombolysis in cerebral infarction

outcomes, the distribution of mRS 3 months post procedure was as follows: 0 in two cases, 1 in one case, 2 in ten cases, 3 in one case, 4 in eleven cases, 5 in one case, and 6 in three cases. The cause of death for cases with mRS score 6 at 3 months post procedure was pneumonia. As a result, good and poor prognoses were achieved in 13 (45%) and 16 (55%) patients, respectively. Comparisons between two groups showed significant differences in TICI 3 (8/13 [61.5%] and 2/16 [12.5%] in good and poor prognosis groups, respectively, $p = 0.016$) and onset to reperfusion (O2R) (213 min [198–271 min] in good prognosis and 315 min [238–486 min] in poor prognosis, $p = 0.004$); however, there was no significant difference in 1 pass TICI 3 ($p = 0.40$) (**Table 1**).

A summary of the logistic regression analysis is presented in **Table 2**. Univariate logistic regression analysis revealed that TICI 3 (odds ratio [OR], 11.2; 95% confidence interval [CI], 2.1–93.8; $p = 0.0107$), O2R (OR, 0.99; 95% CI, 0.98–0.998; $p = 0.0492$), and female (OR, 0.14; 95% CI, 0.02–0.75; $p = 0.0333$) were significantly associated with good outcomes. The combined technique was not significant but showed a trend associated with poor prognosis (OR, 0.23; 95% CI, 0.03–1.26; $p = 0.11$). Multivariate analysis indicated that TICI 3 was associated with good outcomes (OR, 11.7; 95% CI, 1.003–136; $p = 0.0497$) and this association was statistically significant.

Regarding primary MT strategy, a good prognosis was achieved in seven (50%) patients in the SR group, four (66.7%) patients in the AC group, and two (22.2%) patients in the combined technique group; however, the difference between the groups was not statistically significant (**Table 3**).

Discussion

In our retrospective cohort, good functional outcomes (mRS ≤2 at 3 months) were achieved in 13 (44.8%) of the 29 patients with MT for their M2 occlusion. The rates of successful reperfusion, TICI 3, PPH, and symptomatic PPH were 82.8, 34.5, 31.0, and 0%, respectively. Based on multivariate analysis in this cohort, TICI 3 appeared as a prognostic factor of MT for M2 occlusions.

According to the American Heart Association/American Stroke Association guidelines, for patients with acute M2 or M3 segment occlusion, SR is a reliable technique and treatment can be initiated within 6 hours from symptom onset (class of recommendation IIb).[2] Another study reported that MT was associated with favorable outcomes compared to that of the best medical treatment, including intravenous tPA in patients with M2 occlusions.[18] Therefore, scientific evidence regarding MT for M2 occlusions has accumulated, and its efficacy and safety have been established. Our study exhibited satisfactory outcomes;

good functional outcome, PPH, and symptomatic PPH were observed in 44.8%, 31.0%, and 0% of patients, respectively. In the literature, previous studies have reported that good functional outcome, PPH, and symptomatic PPH were observed in 48.6%–65%, 40.5%–42.1%, and 2.6%–9.3% of patients, respectively.[19–21] The results of our retrospective cohort were not inferior to those reported in previous studies. This study showed that MT for M2 occlusion is a reliable and safe procedure.

A prognostic factor of MT for M2 occlusions was TICI 3, based on a multivariate analysis in this cohort. TICI 2c or 3 has been associated with favorable outcomes in LVO.[22–24] However, few studies have reported that TICI 3 is a favorable prognostic factor for M2 occlusion. Our study showed that TICI 2b is insufficient in MT for M2 occlusions, and a strategy aiming for TICI 3 is warranted. In other reports, the efficacy of one-pass TICI 3 recanalization (first-pass effect [FPE]) has been reported in LVO.[25] Although this cohort was small and did not show significant results, it may be possible to validate the efficacy of FPE if the number of cases is large. In future, strategy aiming for one-pass TICI 3 may also be required for MT in MeVO including M2 occlusions. However, achievement of TICI 3 by multiple passes may have risk of hemorrhagic complications. Insisting TICI 3 may not be a good treatment policy. Termination conditions for each procedure should be decided beforehand.

Our results showed that it is important to select a first-line MT strategy aiming for TICI 3 recanalization for M2 occlusion. In MT for LVO, the combined technique can achieve higher rates of FPE.[26] However, no reports have shown that the combined technique has better functional results than those of the SR or AC strategies for LVO. The results of the combined technique group in our cohort were not favorable either radiographically or functionally. The good functional outcome, PPH, and symptomatic PPH were achieved in 22.2%, 55.6%, and 0% of patients, although the difference did not exhibit a statistically significant difference (p = 0.10, **Table 1**). Catheter behavior might be unstable in the M2 segment because of the tortuous anatomy and small caliber.[20,27] Additionally, the estimated thrombus volume in patients with acute ischemic infarction in M2 is smaller than that in the distal portion of the internal carotid artery and the first segment of the MCA (M1).[28] One potential advantage of the combined technique is the retrieval of larger clots. As for MT for M2 occlusions, this merit may not be great, and it may be preferable to select a simpler technique, such as AC or SR, as the first-line strategy. However, the combined technique that uses AC as DAC may increase efficacy and safety of each procedure. The causes of hemorrhagic complication in MeVO may include vascular traction by SR.[29,30] The combined technique that uses AC as DAC may have efficacy in compensating this condition, and there is room for further consideration on the practical techniques of the combined technique. Strategies for achieving TICI 3 recanalization for M2 occlusion should be discussed separately from the evidence accumulated in LVO studies, and more studies focusing on MeVO are warranted.

This study had several limitations. First, it was a retrospective study; therefore, whether the factor reported in this study is truly a prognostic factor should be examined prospectively. Second, the sample size was small, reducing the statistical power. Therefore, some previously reported prognostic factors in MT for M2 occlusions were not significant in this study. Therefore, the treatment results need to be examined in a larger cohort. Third, in this retrospective study, interventionists decided MT strategy in each case without predefined case-selection strategy. Therefore, it is possible that the combined technique was selected in patients having more difficulty in effective recanalization. However, these limitations do not decrease the novelty and importance of our study, in which we have analyzed the procedural and functional results of MT for M2 occlusions and demonstrated that TICI 3 was a favorable prognostic factor. Scientific evidence regarding the prognostic factors for MT in M2 occlusion is not yet established. To improve outcomes to benefit patients, it is important to select appropriate patients and treat them with appropriate thrombectomy techniques.

Conclusion

MT for M2 occlusion is a reliable and relatively safe procedure. TICI 3 was a prognostic factor in this cohort. Future studies using larger cohorts are warranted to investigate the prognostic factors and appropriate MT strategies for M2 occlusions in more detail.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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