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RESEARCH

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Outcomes and safety of mechanical thrombectomy, alteplase, and conventional medical care in the treatment of acute M2 segment middle cerebral artery occlusion: a comparative study

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Abstract

Background Data on mechanical thrombectomy (MT) to treat M2 occlusions of the middle cerebral artery (MCA) are sparse. We report the outcome and safety of MT versus intravenous recombinant tissue plasminogen activator (IV rTPA) versus conventional medical treatment (CMT) of acute ischemic stroke (AIS) due to occlusion of the M2 segment of the MCA. This prospective longitudinal intervention study compared the outcomes and safety of MT, rTPA, and CMT in M2 occlusion AIS patients. National Institutes of Health Stroke Scale (NIHSS), modified Rankin scale (mRS), and recanalization rate assessed outcomes.

Results 74 AIS patients were recruited (23 MT, 23 rTPA, 28CMT). MT group had significantly higher admission NIHSS ($p=0.018$) and mRS ($p=0.023$) than rTPA. At 24 h, NIHSS improved more with MT and rTPA than CMT ($p<0.0001$). At 3 months, mRS were better with MT and rTPA versus CMT ($p<0.0001$). Successful recanalization occurred in 73.9% of the MT group. 69% of the MT group required stent retrieval plus aspiration thrombectomy, and 60.9% required ≥ 3 trials, but outcomes did not differ by technique or number of trials. A good outcome (mRS 0–2) at 3 months was achieved in 69.6% MT versus 65.2% rTPA versus 7.1% CMT ($p<0.0001$). Symptomatic intracranial hemorrhage (sICH) rates were slightly, but insignificantly, higher with CMT. Mortality did not significantly differ between groups.

Conclusions For M2 occlusions, MT and rTPA achieved better early and 3-month outcomes than CMT; however, MT was not superior to rTPA. MT of M2 is feasible and effective, with a lower hemorrhage rate than rTPA and CMT.

Trial registration: This study was prospectively registered in the clinical trial with ClinicalTrials.gov ID (NCT05091320). The link: https://clinicaltrials.gov/study/NCT05091320

Keywords Mechanical thrombectomy, rTPA, M2 segment, Catheter retrieval

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Introduction

Acute ischemic stroke (AIS) is typically categorized into large-vessel occlusion (LVO) and non-LVO. LVOs occur when the proximal arteries in the anterior circulation are occluded [1]. LVOs account for approximately 35–40% of AIS cases, while medium-vessel occlusions (MeVOs) are responsible for 25–40% [2, 3].

MeVO of the middle cerebral artery (MCA) is defined as occlusions of the M2 and M3 segments distinguishing between LVOs and MeVOs can be challenging, particularly when M2 occlusions of the dominant branch produce symptoms similar to M1 occlusions [2–4]. The M2 segment, or insular segment of the MCA, begins at the genu from the first bifurcation of the main MCA trunk, excluding the anterior temporal branch, and ends at the circular sulcus [1]. It comprises branches coursing along the insula within the Sylvian fissure, ascending vertically towards the distal insular circular sulcus before turning sharply to surround the opercula, marking the transition to the M3 segment [5].

Mechanical thrombectomy (MT) has shown superior efficacy to intravenous thrombolysis using intravenous recombinant tissue plasminogen activator (IV rTPA) for M1 occlusions in recent clinical trials [6, 7]. While M2 occlusions exhibit higher revascularization rates with IV rTPA than proximal occlusions, MT may be an effective alternative when rTPA is ineffective or contraindicated [8–10]. Bala and colleagues reported superior clinical outcomes and reduced symptomatic intracranial hemorrhage (sICH) rates for M2 occlusions treated 6–24 h after symptom onset [11]. Similarly, a meta-analysis by Liyis and colleagues showed that patients with M2 occlusions had lower baseline NIHSS scores and better functional outcomes at 90 days, albeit with lower recanalization rates than M1 occlusions [12].

Although MT for MeVO has shown promise as a therapy option, it does include hazards such as vascular perforation and sICH. These studies underscore the importance of careful patient selection and consideration of individual risk factors when performing MT for MeVO [13, 14].

Several studies comparing MT to IV rTPA best medical management (BMM) for distal, medium-vessel occlusions (DMVOs), and M2 segment occlusions have yielded mixed results. Salim and colleagues found no significant difference in functional independence at 90 days between MT and BMM for DMVOs but noted higher rates of hemorrhagic complications with MT [15]. Similarly, Zhou and colleagues reported no statistical difference in favorable outcomes between MT and IV rTPA alone for M2 occlusions, with MT associated with higher rates of subarachnoid hemorrhage and pneumonia [16]. These findings highlight the need for careful patient selection and further research to refine treatment strategies for these specific stroke subtypes [16].

High-level evidence from randomized controlled trials (RCTs) is necessary to establish MT as standard care for MeVO patients. A recent review by Ospel and colleagues summarizes five ongoing MeVO RCTs for endovascular treatment. These trials—DISCOUNT, DISTAL, DISTALS, ESCAPE-MeVO, and FRONTIER-AP—collectively aim to evaluate MT efficacy in MeVOs, with sample sizes ranging from 168 to 530 patients. This review addressed the knowledge gap regarding the optimal management of MeVOs, potentially expanding the indications for endovascular therapy in AIS [17].

Given the current knowledge and the lack of such comprehensive studies comparing all treatment options for M2 occlusions in the Egyptian healthcare context, there is a critical need for region-specific evidence to guide clinical practice. In Egypt, where stroke care resources and practices may differ from those in previously studied populations, a direct comparison of MT, IV rTPA, and conventional medical treatment (CMT) for M2 occlusions is particularly warranted. This study aims to address this need by comparing the efficacy and the short- and long-term outcomes of MT versus IV rTPA versus CMT in AIS patients with occlusion of the M2 division of the MCA.

Methods

This prospective longitudinal study was conducted from December 1, 2021, to November 30, 2023, focusing on AIS due to M2 occlusion of MCA. The study received ethical approval from the [blind] University Faculty of Medicine (IRB 17200628 on 17/10/2021). The clinical trial was registered on ClinicalTrials.gov (NCT05091320). The research adhered to the ethical principles outlined in the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from patients or relatives after explaining all study aspects and potential risks. This study followed the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) [18].

Patients were recruited consecutively from the emergency departments of two University hospitals during the same time period. At [blind] University Hospitals, patients with AIS were selected if they met the eligibility criteria for MT according to established guidelines [19]. At [blind] University Hospitals, patients were included if they were either eligible for rTPA based on guidelines [19] or CMT if rTPA was unavailable or if they arrived at the hospital beyond the 4.5-h window from stroke onset required for rTPA administration.

The general inclusion criteria for the three groups encompassed patients aged between 18 and 70 years who

had cerebral infarction due to M2 occlusion of the MCA. The exclusion criteria included proximal MCA occlusion or cases where the occlusion was initially more proximal and then propagated distally, a history of stroke in the 3 months before, the presence of comorbidity (renal, liver, blood disease, or others), and patients refusing to participate in the study. Additional criteria for rTPA followed the National Institute of Neurological Disorders and Stroke (NINDS) study [20]. All eligible patients were included in the study during this time frame, ensuring a representative sample without selection bias. No randomization was employed, as MT is a highly specialized treatment and should only be performed at hospitals with experience (blind).

The patients in this study who had AIS secondary to occlusion of the M2 segment of MCA were classified according to treatment modality [19] into three groups: (1) the MT group, the patients were recruited from [blind] University Hospital following AIS. The MT group exclusively comprised patients ineligible for rTPA due to late arrival but eligible for MT (4.5–16 h of onset). Patients with combined LVO and M2 occlusions were excluded. (2) The IV rTPA group comprised patients who were recruited from [blind] University Hospital, arrived at the emergency unit within the time window (4.5 h), and were eligible for IV rTPA. (3) The CMT group, also recruited from [blind] University Hospital, included patients who arrived at the emergency unit outside the rTPA time window and received antiplatelet therapy due to MT unavailability due to lack of equipment or personnel.

Clinical assessment included detailed patient history including demographics (age, sex) and different vascular risk factors (hypertension, diabetes mellitus (DM), atrial fibrillation (AF), hyperlipidemia, smoking, and ischemic heart disease) and confirmed by assessment of these risk factors. All patients were assessed at the time of presentation with the National Institutes of Health Stroke Scale (NIHSS) [21] and modified Rankin scale (mRS) [22]. Laboratory routine investigations included complete blood picture (CBC), random blood sugar, lipid profile, electrolyte level, renal function, and ECG.

The initial imaging assessment involved a CT scan and CT angiography or MR angiography (depending on availability at the time of admission). Patients who exhibited symptoms and radiographic evidence indicating medium-sized occlusions and met the specified clinical criteria for MT underwent a thorough assessment of the arteries in the brain using arterial imaging. The preferred method for this evaluation is computed tomography angiography (CTA) using non-enhanced thin sections helical 16 multidetector CT (GE optima CT scanners made in Chicago, USA). However, magnetic resonance angiography (MRA) can be used as an alternative. Additional imaging included perfusion CT imaging or diffusion-weighted MRI imaging using a 1.5-T scanner (Achieva, Philips, made in Amsterdam, Netherlands) to detect and measure the ischemic penumbra and evaluate patient suitability for MT within the extended time window. These imaging techniques were also used to confirm the M2 segment occlusion.

Treatment protocols included admitting all patients to stroke/intensive care units. The IV rTPA group received Actilyse (Boehringer Ingelheim, Ingelheim, Germany) within 4.5 h of the stroke onset at a dosage of 0.9 mg/kg, administered as a 10% bolus over one minute, followed by the remainder via a one-hour infusion pump [19]. Recanalization was assessed by multisclice CT (MSCT) angiography within 24 h of injection. The CMT groups received antiplatelet medication according to guidelines after missing or unavailable MT tools.

For the MT group, digital subtraction angiography (DSA) by expert neurointerventionists assessed the occlusion site. MT was performed under local anesthesia with conscious sedation and heparinized flush, using individualized thrombectomy devices (stent retrievers, aspiration, or combined) per FDA guidelines [23]. The surgical approach utilized an 8 F soft tip guiding catheter, which was introduced to the petrous part of ICA, an intermediate catheter with stent retriever (Solitaire: Medtronic; FR; ev3 Neurovascular, Irvine, CA), and an aspiration catheter (Sofia 5F: MicroVention Terumo). Data recorded included procedural time, thrombectomy method, trial number, and post-procedure assessment was employed using the Modified Thrombolysis in Cerebral Infarction (mTICI) score [24] to evaluate revascularization, complications, and reperfusion injury. All groups received 3 months of antiplatelet medication and participated in rehabilitation programs [23], according to the deficit.

All participants underwent clinical and neurological evaluations made at admission (baseline NIHSS and mRS), 24 h after treatment (NIHSS), and 3 months later (mRS).

The National Institutes of Health Stroke Scale (NIHSS) is the most frequently used neurological deficit rating scale. Its maximal score is 42 (hypothetical due to the existence of numerous mutually exclusive items), and it encompasses a maximal possible deficit of 42 and a range of 0 (no deficit) [21].

The modified Rankin scale (mRS) assesses the extent of functional neurological disability following a stroke. It encompasses a spectrum of severity, from no symptoms to mild disability (0–2), moderately severe disability (3–4), and severe/death (5–6) [22].

The Modified Thrombolysis in Cerebral Infarction (mTICI) score was used to evaluate the angiographic outcome in the MT group. It ranges from 0 (indicating no reperfusion) to 3 (indicating full reperfusion in the distribution of the occluded artery). The score assesses the recanalization of the original primary occlusive lesion and the reperfusion of the distal vasculature of the occluded artery at the end of the angiographic procedure [24]. Recanalization was considered successful if the post-procedure mTICI score was 2b/3 [25]

Outcome measures: The primary outcome was the percentage of patients who achieved a good functional outcome, defined as a modified Rankin scale (mRS) score of 2 or less at 90 days (functional independence). The clinical neurological outcome was assessed after 24 h using the NIHSS. A good outcome was defined as an NIHSS score of 2 or less or a decrease in NIHSS score of 10 points or more after 24 h. The secondary outcomes were assessed using the presence of symptomatic intracranial hemorrhage (sICH) within 72 h and the mortality rate at 90 days.

Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). The Shapiro–Wilk test assessed normality, and the data were abnormally distributed. Continuous variables were represented by mean ± standard deviation (SD), median, and interquartile range (IQR), while frequencies and percentages represented categorical variables. The Chi-square test of Fisher's exact test was employed to compare categorical variables. The Mann–Whitney *U* test was utilized to compare continuous variables between two groups. The Wilcoxon signed-rank test evaluated pre- and post-treatment changes in NIHSS and mRS scores within groups. The Kruskal–Wallis test was employed to compare continuous variables across the three treatment groups. The Friedman test assessed the time × group interaction for NIHSS and mRS score changes. A two-tailed $p < 0.05$ was considered statistically significant. All *p*-values reported in this manuscript were adjusted for multiple comparisons using the false discovery rate (FDR) correction method.

Results

A total of 120 patients were initially screened for eligibility in this study. After applying the exclusion criteria, 46 patients were excluded: 20 due to proven proximal MCA occlusion, 15 due to internal carotid artery occlusion, 8 who refused to participate, and 3 had missing data (see Fig. 1, flowchart).

Table 1 shows demographic and risk factor data for the three treatment groups. 74 patients met the inclusion criteria and were enrolled in the study. These

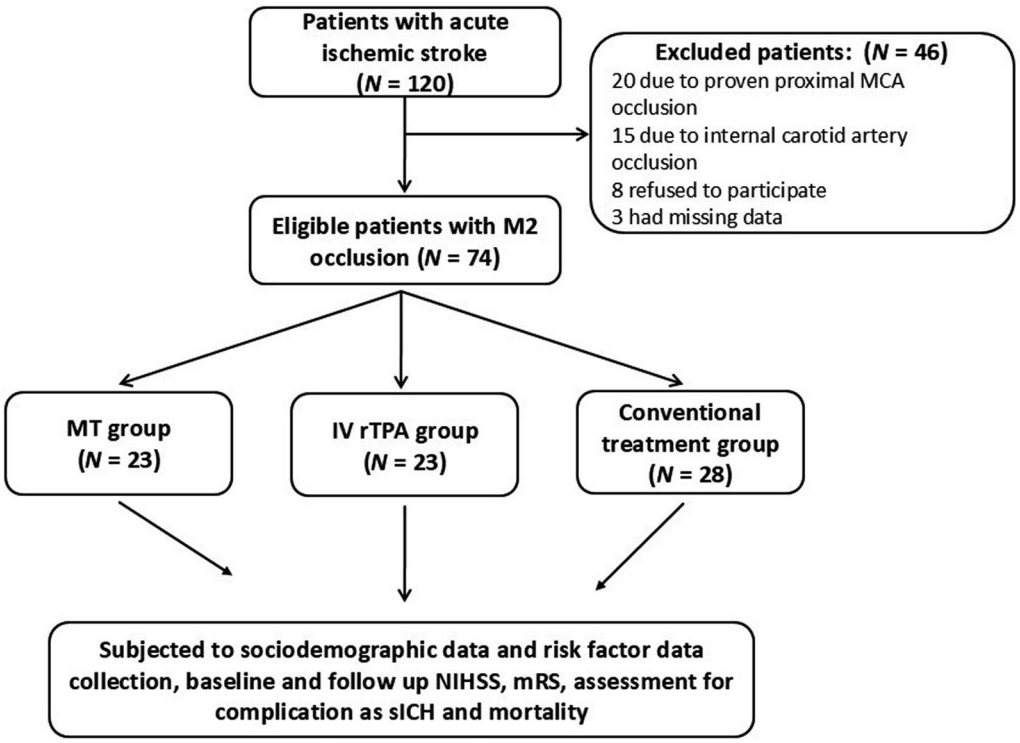

Fig. 1 Flowchart of the study participants

Table 1 Demographic and risk factors among the 3 studied groups

	MT ($n=23$)	Medical treatment		*p* value between the 3 groups	*p* value between MT versus rTPA group	*p* value between MT versus CMT group	*p* value between rTPA versus CMT group
		rTPA ($n=23$)	CMT ($n=28$)				
	Number (%)	Number (%)	Number (%)				
Age (mean ± SD)	59.7 ± 9.758	63.04 ± 10.494	59.64 ± 13.130	0.658	0.350	0.704	0.601
Median (IQR)	60 (12)	63 (14)	63.50 (17)				
Sex male/ female	13/10	14 /9	16/12	1	0.500	0.594	0.507
Risk factors (%)							
Hypertension	18 (78.3%)	13 (56.5%)	18 (64.3%)	0.286	0.104	0.218	0.390
Diabetes mellitus	16 (69.6%)	5 (21.7%)	14 (50%)	0.004	0.001	0.130	0.036
Atrial fibrillation	4 (17.4%)	0 (0%)	8 (28.6%)	0.013	0.054	0.275	0.005
Ischemic heart disease	11 (47.8%)	7 (30.4%)	6 (21.4%)	0.120	0.183	0.45	0.339
Hyperlipidemia	16 (69.7%)	8 (34.8%)	10 (35.7%)	0.029	0.019	0.016	0.590
Smoking	9 (39.1%)	7 (30.4%)	12 (42.9%)	0.691	0.379	0.507	0.268
Clinical rating scales							
NIHSS at admission (mean ± SD)	13.17 ± 3.17	11.17 ± 1.67	11.61 ± 2.59	0.037	0.018	0.057	0.355
Median (IQR)	14 (6)	11 (2)	12 (6)				
mRS at admission (mean ± SD)	4.57 ± 0.73	4.22 ± 0.52	4.29 ± 0.85	0.108	0.023	0.220	0.465
Median (IQR)	5 (1)	4 (1)	5 (1.75)				
Time passed from onset to procedure in minutes							
Onset to groin (mean ± SD)	356.90 ± 79.79	–	–				
Median (IQR)	360 (100)						
Onset to revascularization (mean ± SD)	45.81 ± 12.43	–	–				
Median (IQR)	45 (21)						
Onset to door (mean ± SD)	–	136.77 ± 40.57	–				
Median (IQR)		132.50 (83)					
Onset to needle (mean ± SD)	–	56.95 ± 39.43	–				
Median (IQR)		40 (33)					

Fisher's exact test compares numbers and percentages between groups. The Kruskal–Wallis test compares the means of the three groups

MT: mechanical thrombectomy; CMT; conventional medical treatment group; IQR: interquartile range; n: number of cases; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale; rTPA: recombinant tissue plasminogen activator; SD: standard deviation

patients were then allocated into three treatment groups according to the time window and inclusion and exclusion criteria for each group: 23 received MT, 23 received IV rTPA, and 28 received CMT (see Fig. 1, flowchart). There were no significant differences in terms of age, sex, and some vascular risk factors such as hypertension, ischemic heart disease, and smoking among the three treatment groups. However, there are significant differences observed among the three groups regarding diabetes mellitus (DM) ($p=0.004$), atrial fibrillation (AF) ($p=0.013$), and hyperlipidemia ($p=0.029$). Inter-group comparisons revealed statistically significant differences in some risk factors between groups. The MT group showed a significantly higher prevalence of DM ($p=0.001$) and hyperlipidemia ($p=0.019$) than the rTPA group and CMT ($p=0.016$). The CMT group showed a significantly higher prevalence of DM ($p=0.036$) and AF ($p=0.005$) than in rTPA.

At baseline, the median NIHSS score among the three treatment groups was significantly different ($p=0.037$), while the mRS scores were comparable across groups. The MT group showed a higher median NIHSS score ($p=0.018$) and higher mRS score

Table 2 NIHSS (pre–post 24 h after treatment) and mRS (pre- 3 months after treatment) changes among studied groups

Treatment mode (*n*)	NIHSS at admission	NIHSS after 24 h	Wilcoxon signed ranks test for each group (pre–post treatment)	Friedman measure analysis Time X Group Interaction	mRS at admission	mRS after 3 months	Wilcoxon signed ranks test for each group (pre–post treatment)	Friedman measure analysis Time (pre–post) X 3 Group3 Interaction	*p* value between the changes in MT versus rTPA group		*p* value between changes in MT versus CMT group		*p* value between the changes in rTPA versus CMT group	
									Mann–Whitney test between two groups					
									NIHSS 24 HR	mRS 3 months	NIHSS 24 HR	mRS 3 months	NIHSS 24 HR	mRS 3 months
MT (23)	13.17 ± 3.17	6.32 ± 3.40	< 0.0001	< 0.0001	4.57 ± 0.73	1.64 ± 1.29	< 0.0001	< 0.0001	0.035	0.102	< 0.0001	< 0.0001		
(mean ± SD)	14 (6)	5 (6)			5 (1)	1 (1)								
rTPA (23)	11.17 ± 1.67	4.57 ± 5.38	0.001		4.22 ± 0.52	1.35 ± 1.82	< 0.0001						< 0.0001	< 0.0001
(mean ± SD)	11 (2)	4 (5)			4 (1)	1 (2)								
CMT (28)	11.61 ± 2.59	11.75 ± 3.48	0.72		4.29 ± 0.85	3.43 ± 0.96	0.001							
(mean ± SD)	12 (6)	12 (5)			5 (1.75)	3 (1)								

MT: mechanical thrombectomy; CMT: conventional medical treatment group; IQR: interquartile range; n: number of cases; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale; rTPA: recombinant tissue plasminogen activator; SD: standard deviation

($p = 0.023$) than the rTPA group, indicating more severe initial stroke conditions in the MT group. Other intergroup comparisons were nonsignificant.

The timeline from stroke onset to intervention was assessed in MT and rTPA. In the MT group, the onset-to-groin time was 356.90 ± 79.79 min, and the revascularization time ranged from 20 to 80 min, with a mean of 45.81 ± 12.43 min. In the rTPA group, the onset-to-door time was 136.177 ± 40.57 min, and the onset-to-needle time was 56.95 ± 39.43 min.

Table 2 compares 24-h NIHSS and 3-month mRS outcomes across the three treatment groups. The study revealed significant improvements in neurological outcomes across treatment groups. At 24 h post-intervention, the MT group achieved the greatest reduction (pre–post 24 h) in NIHSS scores ($p < 0.0001$), followed by the rTPA group ($p = 0.001$), while the CMT group showed minimal change in NIHSS scores ($p = 0.72$).

Functional outcomes measured by mRS at 3 months showed significant improvements from admission in both MT and rTPA groups ($p < 0.0001$ for both) and for the CMT group ($p = 0.001$). The Friedman Measure Analysis revealed a significant time x treatment interaction ($p < 0.0001$) for both NIHSS and mRS scores across the three groups.

In intergroup comparisons at 24 h, the rTPA group demonstrated better neurological outcomes with lower NIHSS scores compared to the MT group ($p = 0.035$). Both MT and rTPA groups showed significantly better outcomes than the CMT group ($p < 0.0001$ for both comparisons). At 3 months, MT and rTPA groups achieved comparable mRS scores ($p = 0.102$), and both groups demonstrated significantly better functional outcomes than the CMT group ($p < 0.0001$ for both comparisons).

Table 3 summarizes the safety outcomes, including sICH rates and mortality. The sICH rates ($p = 0.314$) and mortality ($p = 0.837$) were comparable across all three groups. Regarding good functional outcomes at 3 months, both MT (69.6%) and rTPA (65.2%) groups achieved significantly higher rates compared to the CMT group (7.1%) ($p < 0.0001$ for both comparisons). These findings demonstrate that MT and rTPA interventions led to superior patient outcomes compared to CMT.

Table 4 lists details of the MT procedure, including thrombectomy mode, trial number, and mTICI score. Mixed procedures combining stent retrieval and aspiration were used in 69% of cases. Most procedures (60.9%) required three or more trials. Successful recanalization (mTICI 2b/ 3) was achieved in 73.9% (Figs. 2 and 3).

Discussion

In general, the treatment goal for an AIS is to restore blood supply to the afflicted brain region as soon as possible, i.e., within the first few hours following the onset of stroke symptoms.

This prospective longitudinal study aimed to compare the outcomes, effectiveness, and safety of MT, IV rTPA, and CMT for treating M2 MCA occlusions as a selective group of AIS in which the MT was scarce. Our analysis of the three groups suggested several potential trends: (1) patients treated with MT and IV rTPA appeared to have better 24-h NIHSS scores compared to those receiving CMT; (2) MT and IV rTPA groups showed a tendency towards improved 3-month mRS scores (≤ 2) relative to the CMT group; (3) successful recanalization after MT (73.9%) was associated with numerically, though not statistically significant, better NIHSS and mRS outcomes; (4) the observed safety profiles, including rates of sICH and mortality were comparable across the three treatment modalities.

In the current study, the baseline characteristics of the MT group were comparable to the other treatment groups (IV rTPA and CMT) in terms of age and sex distribution. However, the MT group had a higher frequency of DM and hyperlipidemia, while the CMT group had a higher frequency of AF. These observations highlight the importance of optimal management of stroke risk factors and suggest that MT could be advantageous for individuals ineligible for rTPA due to certain risk factors. The increased frequency of AF in the CMT group is likely because many were on anticoagulant therapy, making them ineligible for rTPA. The MT group had a higher NIHSS at admission than the rTPA group, which is similar to the findings of Miura and colleagues [26], who reported that the MT group had a higher baseline score than the rTPA group. Thus, MT may be a second-line treatment for AIS, offering revascularization to high-NIHSS patients ineligible for IV rTPA.

In this study, we did not measure admission glucose levels. However, the high incidence of diabetes, hypertension, and hyperlipidemia among the studied groups may partially explain the poor outcomes. This finding is supported by Bruno and colleagues who found that higher admission blood glucose levels were associated with worse outcomes at 3 months, according to multivariate logistic regression analysis adjusted for stroke severity, diabetes mellitus, and other vascular risks [27].

In the present study, despite MT's higher baseline NIHSS, the MT and IV rTPA groups showed significantly greater improvements in NIHSS scores 24 h following therapy than the CMT group. Also, the MT (69.6%) and IV rTPA (65.2%) groups had better functional outcomes (mRS 0–2) at 3 months compared to the CMT group

Table 3 Comparison of the secondary outcomes among MT, rTPA, and medical treatment groups

Variable of assessment	MT group ($n=23$)	rTPA group ($n=23$)	CMT group ($n=28$)	*p* value between the three groups	*p* value between MT versus rTPA group	*p* value between MT versus CMT group	*p* value between rTPA versus CMT group
Symptomatic intracerebral hemorrhage	2 (8.7%)	4 (17.4%)	7 (25%)	0.314	0.333	0.124	0.379
Mortality at 3 months follow-up	2 (8.7%)	1 (4.3%)	2 (7.1%)	0.837	0.500	0.617	0.575
Good outcome at 3 months follow-up	16 (69.6%)	15 (65.2%)	2 (7.1%)	< 0.0001	0.500	< 0.0001	< 0.0001

Fisher's exact test compares numbers and percentages between groups

CMT: conventional medical treatment group; n: number of cases; MT: mechanical thrombectomy; rTPA: recombinant tissue plasminogen activator; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale

Table 4 Mechanical thrombectomy procedures (mode of thrombectomy, number of trials, and revascularization

Mechanical thrombectomy procedures	Mode/grade/trials	Number (%)
Mode of thrombectomy	Stent retrieval	4 (13%)
	Aspiration	3 (17.4%)
	Mixed procedure	16 (69%)
Number of trials	One trial	1 (4.3%)
	Two trials	8 (34.8%)
	Three or more trials	14 (60.9%)
Grade of recanalization (mTICI score)	No or partial recanalization (mTICI 0/1/2a)	6 (26.1%)
	Successful recanalization (mTICI 2b/3)	17 (73.9%)

mTICI: thrombolysis in cerebral infarction

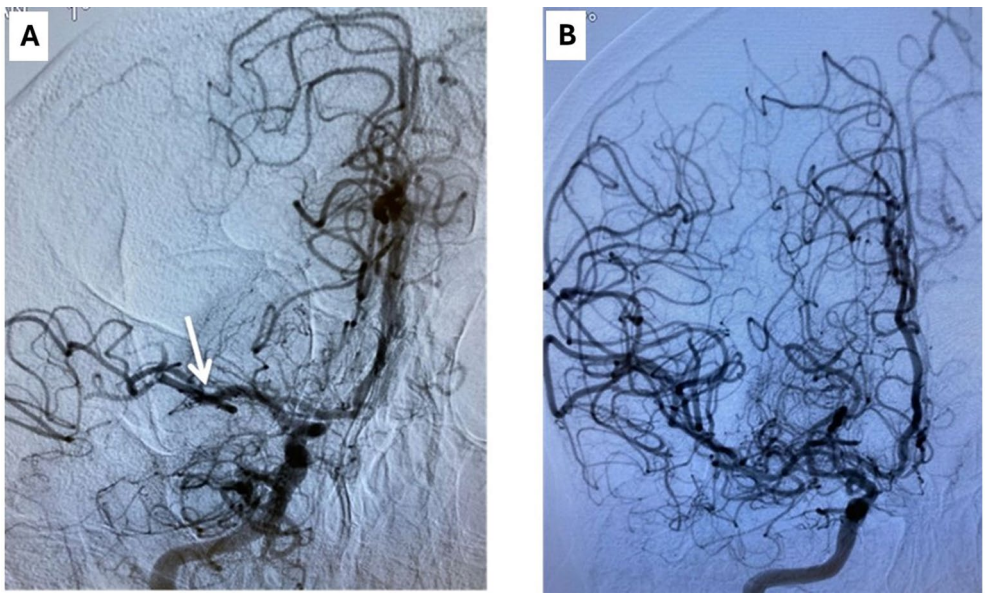

Fig. 2 A 64-year-old male patient with NIHSS 8. Digital subtraction angiography (DSA) anteroposterior view (**A**) demonstrates left MCA M2 (superior division) occlusion (arrow). Mechanical thrombectomy was performed using the combined technique of thrombus aspiration and stent retrieval using the Sofia aspiration and Solitaire stent retrieval system. After two attempts, the mTICI 3 score was achieved, as demonstrated at DSA anteroposterior view (**B**), and the NIHSS 2 was achieved on discharge

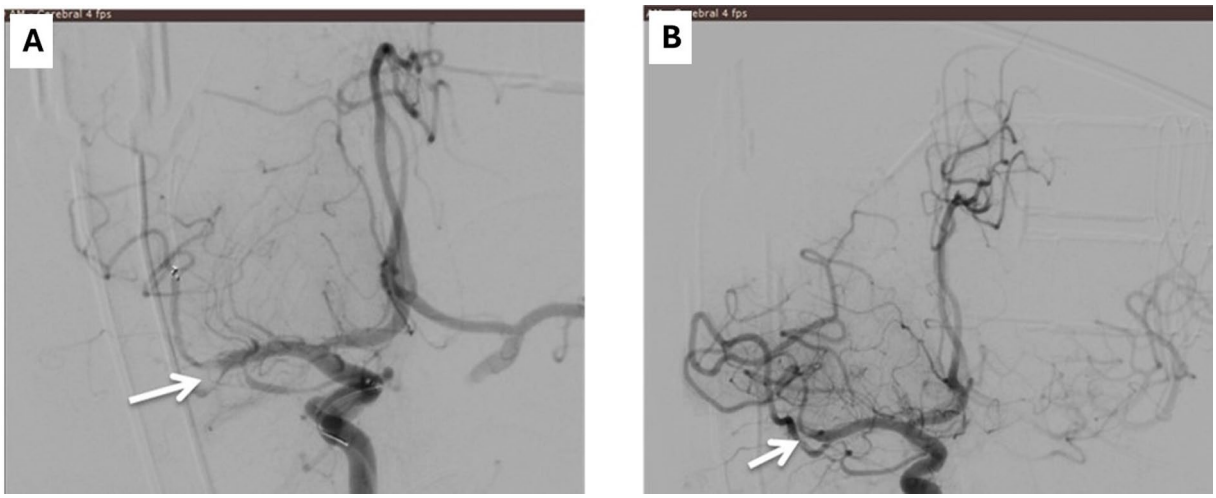

Fig. 3 A 58-year-old female patient with NIHSS 14, digital subtraction angiography (DSA) anteroposterior view demonstrates right M2 occlusion (arrow) (**A**). Mechanical thrombectomy was performed using the combined technique (thrombus aspiration and stets retrieval) using the Sofia thrombus aspiration device and Solitaire stent retrieval device. Successful recanalization with mTICI 2b score was achieved on the DSA anteroposterior view (arrow) (**B**), and the NIHSS 3 was achieved on discharge

(7.1%). These findings suggest that MT and IV rTPA interventions may be equally efficacious treatments for M2 occlusions, achieving comparable neurological outcomes in terms of 24-h NIHSS or 3-month mRS scores. These results corroborate previous research indicating potential long-term advantages of MT for M2 occlusion patients [26, 28–32].

Marchal and colleagues found that MT improved neurological and functional results for distal M2 occlusions compared to medical management [29]. A recent meta-analysis by Barchetti and colleagues revealed an overall good functional outcome rate of 58.8% at the 3-month follow-up for MT in distal locations [33]. Vidale and colleagues (2021) conducted a systematic review and meta-analysis, comparing the risk–benefit profiles of MT with or without IV rTPA versus IV rTPA alone in adults with AIS and M2 occlusion. They found similar rates of good functional outcome (mRS < 3) at 90 days between the two strategies, MT versus IV rTPA (62.4% versus 66.3%, respectively) [32]. Moreover, Waqas and colleagues (2021), in their meta-analysis of patients who underwent MT for distal circulation strokes, found that 54.7% of patients who had MT achieved a favorable outcome at 3 months, which was comparable to the 54.5% of IV rTPA [34]. Furthermore, Guo and colleagues (2023) demonstrated in their meta-analysis that MT was associated with better functional outcomes (mRS 0–2) than best medical management in patients with M2 occlusion and moderate-to-severe stroke [28].

The current result suggests the potential benefits of MT in improving functional outcomes and reducing long-term disability in patients with DMVOs, which are often associated with poor prognosis when treated with CMT alone. These findings align with those of Menon and colleagues who reported improved functional independence in patients with M2 segment occlusion who received MT at 90 days compared to those who received the best medical treatment [30]. Similar effects were reported by Sarraj and colleagues (2016) and Miura and colleagues (2019), underscoring the superiority of MT management for M2 occlusions [26, 31].

sICH is the most feared complication of MT [35], especially in smaller vessels which are more vulnerable when treated endovascularly. Saber and colleagues (2018) conducted a meta-analysis of 1080 patients who underwent M2 thrombectomy, comparing them to those with M1 occlusions. The analysis suggests that M2 thrombectomy may carry an increased risk of sICH risk [36]. In the current study, the sICH rates across the three treatment groups appeared to show no notable differences. This observation is consistent with findings from previous studies [29–31, 37]. Menon and colleagues found no sICH in patients treated with MT for M2 occlusions compared with a 7.9% rate in the best medical management group (IV-tPA) [30]. Marchal and colleagues reported that sICH occurred in 3.1% of the MT group and 9.5% of the non-MT group [29]. Conversely, Vidale and colleagues found a higher sICH rate in the MT group (8.5%) compared to the IVT group (3%) [32]. Waqas and colleagues reported that 5.8% of patients who underwent MT for strokes in the distal locations experienced sICHs, comparable to 2.5% of patients treated with IV tPA [34].

In the present study, the mortality rate in the MT group appeared to be comparable with that of the other

treatment groups, supporting the safety of this treatment modality, as shown in previous studies [26, 28, 37]. Miura and colleagues reported that MT was associated with lower mortality than medical management in a real-world cohort of patients with M2 occlusions [26]. However, Waqas and colleagues reported a 16.5% mortality rate for MT, comparable to 12.4% for IV tPA in treating strokes in distal locations [34]. It is important to consider the potential for susceptibility bias, as patients selected for MT were likely "sicker" and thus had a higher risk of mortality. Residual confounding may also influence these outcomes. Conducting RCTs is essential for more definitive conclusions.

Regarding the procedural aspects of MT, in this study, the subgroup analysis of the MT group suggests potential insights into the technical aspects of MT for M2. Most cases required a combination of stent retrieval and aspiration techniques, reflecting the complexity of these distal occlusions. Furthermore, multiple thrombectomy attempts were often required, with nearly 61% of cases requiring three or more passes. This may highlight some challenges associated with navigating and recanalizing these small intracranial vessels. However, given the limited sample size, these observations should be interpreted cautiously and may warrant further investigation in larger studies.

While providing initial insights into MT for the M2 segment of MCA occlusions, this study has several limitations. First, the limited sample size constrains the statistical power and generalizability of our findings. Second, the non-randomized, observational design introduces potential selection bias and confounding variables. Third, there is a possibility that patients selected for more aggressive interventions like mechanical thrombectomy had different baseline clinical characteristics, potentially influencing outcomes independently of the treatment effect. Fourth, the absence of perfusion imaging due to resource constraints limits our ability to assess cerebral blood flow comprehensively. Fifth, the study lacks a direct comparison to intra-arterial thrombolysis and does not explore the impacts of precise lesion location, collateral circulation, or time to revascularization. Finally, the absence of long-term follow-up beyond 3 months restricts our understanding of the sustained effects of the treatments. These limitations underscore the need for cautious interpretation of our findings and highlight the importance of future RCTs in establishing causal relationships and more effectively controlling for potential confounding factors.

To address these limitations, future large-scale, multicentre RCTs with perfusion imaging, particularly perfusion mismatching, are recommended to validate findings, compare endovascular treatment modalities, identify predictors of successful recanalization and favorable outcomes, refine patient selection criteria, and optimize treatment strategies for M2 occlusions to help improve patient outcomes. Such trials would provide more robust evidence to guide clinical decision-making in managing M2 MCA occlusions.

Conclusions

This study suggests that MT and IV tPA are safe and effective treatments for M2 occlusions of MCA, with better neurological and functional outcomes than medical management. MT may be beneficial for this subset of stroke patients who are ineligible or unresponsive to standard rTPA. However, larger RCTs are needed to validate the findings and explore optimal treatment strategies, considering factors like lesion location, time to revascularization, and adjunctive therapies.

Abbreviations

ACA	Anterior cerebral artery
AF	Atrial fibrillation
AIS	Acute ischemic stroke
CBC	Complete blood count
CT	Computed tomography
CTA	Computed tomography angiography
DM	Diabetes mellitus
DSA	Digital subtraction angiography
ECG	Electrocardiogram
FDA	Food and Drug Administration
HTN	Hypertension
ICA	Internal carotid artery
IV rTPA	Intravenous recombinant tissue plasminogen activator
LVO	Large vessel occlusion
MCA	Middle cerebral artery
MeVO	Medium vessel occlusion
mRS	Modified Rankin scale
MT	Mechanical thrombectomy
NIHSS	National Institutes of Health Stroke Scale
PCA	Posterior cerebral artery
sICH	Symptomatic intracranial hemorrhage
mTICI	Modified thrombolysis in cerebral infarction

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Author contributions

EMK: study conceptualization and design, data analysis, manuscript reviewing and editing. AEB: study conceptualization and design, methodology, manuscript reviewing and editing. MN: data collection, methodology, manuscript reviewing and editing. AA: preparing Figs. 2 and 3, original draft writing, manuscript reviewing and editing. KOM: study conceptualization and design, manuscript reviewing & editing. NAH: data analysis, preparing Fig. 1, original draft writing, manuscript reviewing and editing. All authors have read and approved the final version of the manuscript to be published.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the Assiut University, Faculty of Medicine's ethical committee and registered with the Institutional Review Board (IRB no: 17200628). The clinical trial was registered on ClinicalTrials.gov (NCT05091320). The research adhered to the ethical principles outlined in the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from patients or relatives after explaining all study aspects and potential risks.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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