Middle Cerebral Artery M2 Segment Occlusion Treatment

- M2 vessel occlusion characteristics and outcome after endovascular therapy: A post-hoc pooled analysis of MR CLEAN MED, NO-IV and LATE
- Effects of body mass index on functional outcomes in patients with acute cerebral large vessel occlusion
- Treatment outcomes of successful M1 versus M2 thrombectomy for low-ASPECTS stroke patients
- Association between M1 tortuosity and intracranial hemorrhage after mechanical thrombectomy using a stent retriever for M2 occlusions
- Comparing clinical outcomes in patients with M2 middle cerebral artery segment occlusions of different stroke etiologies who undergo endovascular treatment: A retrospective study
- Endovascular Therapy for Late-Window M2-Segment Middle Cerebral Artery Occlusion: Analysis of the CLEAR Study
- A Case of Partially Thrombosed Dissecting Giant Aneurysm in the Distal Middle Cerebral Artery Treated by Endovascular Parent Artery Occlusion
- Safety first: A comparative study of mechanical thrombectomy techniques for M2 occlusions - stent-retriever thrombectomy (SRT) vs. first stenting without retrieval (FRESH)

Definition

The **M2 segment** of the middle cerebral artery (MCA) refers to the **insular segment**. Occlusions in this area can cause significant ischemic strokes despite involving smaller vascular territories than M1.

Standard Treatment Options

Intravenous Thrombolysis (IVT)

- **Alteplase (tPA)** within **4.5 hours** of onset
- May serve as monotherapy or **bridging to EVT**
- Less effective for large clot burdens

Endovascular Therapy (EVT)

- **Mechanical thrombectomy** using stent retrievers or aspiration devices
- Initially reserved for **M1 occlusions**, now supported in select **M2 cases**
- Particularly in:
  - **Disabling deficits**
  - **Good collaterals**
  - **Mismatch on perfusion imaging**
  - **Late window (6–24h)** per DAWN/DEFUSE-3

EVT Selection Criteria

- **NIHSS >6**
- **Small infarct core**, **large penumbra**
- **Good pre-stroke mRS (0–2)**
- **Proximal M2** occlusion more favorable
- **Anatomically accessible**

Imaging Workflow

- **Non-contrast CT** – rule out hemorrhage
- **CT Angiography (CTA)** – identify M2 occlusion
- **Perfusion imaging (CTP or DWI/PWI MRI)** – assess for salvageable brain tissue

Evidence Summary

- The **CLEAR study (2025)** supports EVT for **late-window M2 occlusions** in well-selected patients.
- EVT outcomes in M2 occlusion increasingly **comparable to M1** in efficacy and safety.

Clinical Takeaway

> M2 occlusions should be evaluated for **endovascular treatment**, especially when presenting with disabling symptoms and favorable imaging. Emerging data support extending EVT to **distal occlusions** in the **late window** with appropriate selection.

Multinational Retrospective Observational Cohort Studies

A Multinational Retrospective Observational Cohort Study. Winzer et al. evaluated the clinical outcomes of patients with M2 occlusion selected for EVT compared with those who received medical management (MM) in the late window.

This multinational cohort study was conducted at 66 sites across 10 countries (January 2014 to May 2022). They included consecutive patients with late-window stroke due to M2 occlusion, baseline National Institutes of Health Stroke Scale score of ≥5, and premorbid modified Rankin Scale score of ≤2 who received EVT or MM alone. The primary end point was a 90-day ordinal shift in the modified Rankin Scale score. Safety end points were symptomatic intracranial hemorrhage and 90-day mortality. Differences in outcomes were determined using inverse probability of treatment weighting-adjusted logistic regression models.

Among 5098 patients, 496 met inclusion criteria (median [interquartile range] age, 74 years [62-81 years]; baseline National Institutes of Health Stroke Scale score, 12 [8-17]), of whom 394 (79.4%) received EVT and 102 (20.6%) MM. In inverse probability of treatment weighting adjusted analyses, there was no favorable 90-day ordinal modified Rankin Scale shift (odds ratio, 1.39 [95% CI,

0.92-2.12]) and no difference of functional independence rates (modified Rankin Scale score of 0-2; odds ratio, 1.72 [95% CI, 0.93-3.15]) with EVT compared with MM. Moreover, symptomatic intracranial hemorrhage risk (odds ratio, 3.46 [95% CI, 0.50-23.92]) and 90-day mortality (odds ratio, 1.11 [95% CI, 0.66-1.87]) were not statistically different between treatment groups.

In patients with M2 occlusion in the 6- to 24-hour time window, there was no difference in disability outcomes or symptomatic intracranial hemorrhage risk between patients treated with EVT compared with MM. Results of ongoing randomized trials will provide further insight.

Registration: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04096248 [1)]

Methodological Strengths Large multicenter data across multiple healthcare systems.

Rigorous IPTW-adjusted logistic regression to reduce treatment allocation bias.

Clinically relevant endpoints (ordinal mRS, ICH, mortality) aligned with prior EVT trials.

Methodological Limitations Residual confounding: Despite IPTW, unmeasured variables likely influenced treatment assignment (e.g., infarct core volume, collateral quality).

Selection bias: EVT patients likely differed systematically from MM patients in ways not fully captured by adjustment models.

Imprecision: Wide confidence intervals limit definitive interpretation, especially for safety endpoints.

Lack of imaging core lab adjudication: No mention of centralized imaging assessment for occlusion localization or perfusion mismatch, which are key in late-window decisions.

Temporal heterogeneity (2014–2022): Advances in EVT technique and triage during this period may affect outcome interpretation.

Clinical Relevance The study raises important questions about the real-world effectiveness of EVT for M2 occlusions in late time windows, a subgroup often excluded or underrepresented in trials like DAWN or DEFUSE-3. The absence of harm and potential benefit in selected patients supports a case-by-case decision-making approach until randomized data are available.

Implications and Future Directions Supports equipoise for ongoing RCTs on EVT in distal occlusions and extended time windows (e.g., NCT04096248).

Highlights the need for better imaging biomarkers and standardized triage protocols for EVT in M2 occlusions.

Suggests that the benefit of EVT in this setting may exist, but is more nuanced and requires precise patient selection.

Conclusion

While this well-conducted retrospective study does not show statistically significant differences in outcomes between EVT and MM in late-window M2 occlusions, it hints at a potential clinical benefit without added risk. However, due to methodological limitations and imprecise estimates, the findings should be interpreted cautiously. Randomized trials remain essential to guide definitive treatment

strategies in this increasingly relevant subgroup of stroke patients.

1)

Winzer S, Kaiser DPO, Qureshi MM, Castonguay AC, Strbian D, Nogueira RG, Nagel S, Raymond J, Abdalkader M, Demeestere J, Marto JP, Yamagami H, Tanaka K, Sheth SA, Dusart A, Michel P, Olive Gadea M, Ribo M, Zaidat OO, Haussen DC, Henon H, Mohammaden MH, Möhlenbruch MA, Siegler JE, Puri AS, Kaesmacher J, Klein P, Tomppo L, Caparros F, Ramos JN, Jumaa M, Zaidi S, Martinez-Majander N, Nannoni S, Vandewalle L, Bellante F, Galecio-Castillo M, Salazar-Marioni S, Virtanen P, Wouters A, Ventura R, Jesser J, Mujanovic A, Shu L, Qureshi A, Qiu Z, Masoud HE, Requena M, Sillanpää M, Hu W, Lin E, Cordonnier C, Roy D, Yaghi S, Strambo D, Fischer U, Ortega-Gutierrez S, Lemmens R, Ringleb PA, Nguyen TN, Puetz V. Endovascular Therapy for Late-Window M2-Segment Middle Cerebral Artery Occlusion: Analysis of the CLEAR Study. Stroke. 2025 May 22. doi: 10.1161/STROKEAHA.124.048840. Epub ahead of print. PMID: 40405459.