Original research

# Mechanical thrombectomy in minor stroke due to isolated M2 occlusion: a multicenter retrospective matched analysis

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## ABSTRACT

**Background** The purpose of this study was to evaluate the effectiveness of mechanical thrombectomy (MT) in patients with isolated M2 occlusion and minor symptoms and identify possible baseline predictors of clinical outcome.
**Methods** The databases of 16 high-volume stroke centers were retrospectively screened for consecutive patients with isolated M2 occlusion and a baseline National Institutes of Health Stroke Scale (NIHSS) score ≤5 who received either early MT (eMT) or best medical management (BMM) with the possibility of rescue MT (rMT) on early neurological worsening. Because our patients were not randomized, we used propensity score matching (PSM) to estimate the treatment effect of eMT compared with the BMM/rMT. The primary clinical outcome measure was a 90-day modified Rankin Scale score of 0–1.
**Results** 388 patients were initially selected and, after PSM, 100 pairs of patients receiving eMT or BMM/rMT were available for analysis. We found no significant differences in clinical outcome and in safety measures between patients receiving eMT or BMM/rMT. Similar results were also observed after comparison between eMT and rMT. Concerning baseline predicting factors of outcome, the involvement of the M2 inferior branch was associated with a favorable outcome.
**Conclusion** Our multicenter retrospective analysis has shown no benefit of eMT in minor stroke patients with isolated M2 occlusion over a more conservative therapeutic approach. Although our results must be viewed with caution, in these patients it appears reasonable to consider BMM as the first option and rMT in the presence of early neurological deterioration.

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

⇒ The appropriateness of mechanical thrombectomy in patients with minor stroke due to isolated occlusion of the M2 segment of the middle cerebral artery is controversial.

**WHAT THIS STUDY ADDS**

⇒ Our retrospective study has shown no benefit of upfront mechanical thrombectomy in a large cohort of these patients compared with a more conservative approach based on best medical management with the possibility of a rescue mechanical thrombectomy on early neurological worsening.

**HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY**

⇒ Our study adds further information for the definition of the most effective acute treatment in minor stroke patients harboring more peripheral occlusions of the middle cerebral artery. Nonetheless, this issue remains open for clarification and it is expected that forthcoming randomized controlled trials will provide an unambiguous recommendation in clinical practice.

## INTRODUCTION

Results from randomized trials have defined mechanical thrombectomy (MT) as the standard of care in patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO) in the anterior circulation.[1] Current guidelines recommend MT in patients with a causative occlusion of the internal carotid artery and/or the M1 segment of the middle cerebral artery (MCA) having a baseline National Institutes of Health Stroke Scale (NIHSS) score ≥6 and a pre-event modified Rankin Scale (mRS) score <2.[2] MT is also associated with high rates of favorable outcome in isolated M2 occlusions, although with an increased risk of brain bleeding events.[3–6]

The benefit of MT in patients with AIS due to LVO in the anterior circulation and minor baseline symptoms (NIHSS score ≤5) still needs clarification, as very few patients with minor stroke were included in the main clinical trials and uneven evidence comes from retrospective studies.[1 7–10] The main concern in these patients is the risk of early neurological worsening, and possibly long-term disability, if not subjected to an efficient recanalization procedure.[7 10 11] However, rescue MT performed immediately after clinical deterioration seems to ameliorate, at least in part, the final outcome.[7 10 12] In real-world practice, the decision to perform MT in patients with LVO and a baseline NIHSS score ≤5 is usually considered on a case-by-case basis and after careful assessment of clinical and radiologic features (eg, presence of disabling symptoms, site of occlusion, and vascular anatomy). In this regard, the involvement of the M2 segment, that can be less accessible and expected to lead to a smaller volume of brain infarct, may raise further skepticism about the appropriateness of early MT as acute treatment.

Here we report a large retrospective multicenter analysis on consecutive patients with minor AIS due to isolated occlusion of the M2 segment. The primary purpose of this study was to compare the outcome of patients receiving MT with an NIHSS score ≤5 at the time of groin puncture with the outcome of patients who were kept on best medical management (BMM) only or subjected to rescue MT on neurological worsening after BMM. The secondary aim was to identify possible baseline predictors of clinical outcome in patients with a minor stroke and M2 occlusion that can be valuable when deciding the most appropriate type of treatment.

## METHODS

### Patients and treatment

In this retrospective observational study, the prospective databases of 16 high-volume stroke centers were screened for consecutive patients with AIS due to LVO diagnosed between January 2016 and December 2021.

All patients were diagnosed with a comprehensive head and neck CT protocol consisting of an initial basal scan with determination of the Alberta Stroke Program Early CT (ASPECT) score,[13] followed by CT angiography to locate the site of occlusion. Whenever appropriate, the protocol was implemented with a CT perfusion study to establish eligibility for MT.[2] The identification of the M2 segment involvement was done on CT angiograms according to previous descriptions, and defined as an occlusion located from the genu of the MCA on to the proximal part of one of the first order branches (superior or inferior in cases of bifurcation, and superior, middle or inferior when trifurcation occurred). Caliber dominance was considered present when one division had a larger caliber than the other(s) or, if the occlusion involved the vessel from its origin, if the missing MCA territory was >50%.[6 14 15] Patients with an occlusion site other than the isolated M2 segment, a baseline NIHSS score ≥6, a pre-event mRS score >1 or with incomplete records were excluded.

Patients with M2 occlusion were divided into two cohorts according to the type of treatment that was used. Patients receiving MT with an NIHSS score ≤5 at the time of groin puncture, either preceded or not by intravenous thrombolysis (IVT) according to current guidelines,[16] were defined as the early MT (eMT) group. The control group included patients receiving BMM only (including IVT when applicable) and those initially receiving BMM and then subjected to rescue MT (rMT) on early neurological deterioration (BMM/rMT group). Early neurological deterioration (END) was defined as an increase of NIHSS score ≥4 points from baseline leading to an NIHSS score ≥6 at the time of groin puncture. Treatment decision was based on the individual center's protocol and the managing physician's discretion.

MT was performed with a stent retriever and proximal guide catheter aspiration, direct contact aspiration, or a combination of stent retriever and distal aspiration, at the discretion of each individual interventionalist. Flow restoration at the end of each procedure was graded using the modified Treatment In Cerebral Infarction (mTICI) scale and based on the percentage reperfusion of the territory supplied by M2,[17 18] with successful MT corresponding to a score of 2b-3. In each participating center, two neuroradiologists with more than 5 years of experience and blinded to clinical outcome reviewed the diagnostic radiological and angiographic data of their patients. In cases of doubt or disagreement, DICOM (digital imaging and communications in medicine) images were sent to two expert neuroradiologists of the coordinating center for re-evaluation and adjudication.

### Clinical variables and measures of outcome

Demographic data (age and gender), cardiovascular risk factors and imaging data as well as therapeutic procedures of the acute phase were collected. Clinical outcome was measured with the mRS score acquired at 90 days either in person or on the telephone. A 90-day mRS score of 0–1 (excellent neurological outcome) was chosen as the primary clinical outcome measure given the baseline condition of patients, characterized by mild symptoms. The secondary clinical outcome measure was a 90-day mRS score of 0–2 (functional independence). Safety outcome measures were: (1) brain bleeding events following recanalization therapies, assessed by CT scan or MRI at 72 hours and classified according to previously established criteria[19]; and (2) death of any cause within 90 days after stroke.

### Statistical analysis

Standard descriptive statistics were used to measure central tendency and variability of baseline characteristics.

Since our patients were not randomized, we used propensity score matching (PSM) to estimate differences in outcome measures between patients subjected to eMT versus those undergoing BMM with the possibility of rMT on worsening of clinical conditions, and between patients subjected to eMT versus those receiving rMT, accounting for differences in baseline variables. Covariates included in PSM were age, baseline NIHSS score, pre-event mRS score, occlusion of a dominant M2 division, left-sided stroke, and IVT. Using this model, we calculated the propensity score for each patient. The 'greedy nearest neighbor' matching method was used to find pairs of observations that had very similar propensity scores, setting a caliper of 0.02, as previously described.[20] PSM balance was assessed by checking standardized mean differences between covariates, with a value <0.1 indicating negligible imbalance between treatment groups (online supplemental table 1). We examined differences by the Mann-Whitney U test, Welch two-sample t-test, or $\chi^2$ test as appropriate.

To identify possible predictors of clinical outcome, all collected baseline characteristics were compared in univariate analysis between patients of the entire population with the primary favorable neurological outcome (mRS 0–1) and unfavorable outcome (mRS 2–6), respectively. Comparisons were made using Mann-Whitney U test, Welch two-sample t-test, or $\chi^2$ test as appropriate. Thereafter, to adjust the effect size for potential confounders, a multivariate binary logistic regression analysis was performed, using favorable outcome as the dependent variable and a set of covariates selected for significance in the univariate comparison ($p<0.05$) or for clinical relevance. Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated. The goodness of fit for the logistic regression model was evaluated with the Hosmer-Lemeshow test.

Observed differences were considered significant at a value of $p<0.05$. All analyses were performed using R software v.4.1.3 (https://www.r-project.org).

## RESULTS

A total of 10 169 consecutive patients with AIS due to LVO were screened and 388 patients (189 females, 48.7%) with isolated M2 occlusion, a baseline NIHSS score ≤5, and a pre-event mRS score ≤1 were available for analysis. A flow diagram of patient selection is provided in online supplemental figure 1. Of these, 180 patients (87 females, 48.3%) received MT when having an NIHSS score ≤5 at the time of groin puncture (eMT group). The control group included 121 patients (56 females, 46.3%) who received BMM only and 87 patients (46 females, 52.9%) initially receiving BMM but who later underwent rMT on deterioration of their neurological condition (BMM/rMT group, 208 patients, 102 females, 49%).

Demographics and baseline clinical, radiological, procedural and outcome data of the two cohorts are reported in table 1. Median (IQR) baseline NIHSS score was higher in the eMT group (4 (2–5) vs 3 (2–5), $p<0.001$). Involvement of a dominant M2 division occurred more frequently in the eMT group (66.7% vs 51.9% in the BMM/rMT group, p=0.005). IVT was performed in 54 patients of the eMT group (30%), and in 133 patients of the BMM/rMT group (63.9%, $p<0.001$). Successful reperfusion was achieved in 86.1% of patients in the eMT group and in 89.6% of patients receiving rMT in the control group (p=0.671). Crude rates of 90-day excellent neurological outcome and functional independence were similar between the two treatment groups (mRS 0–1, 81.1% in the eMT group and 78.4%, p=0.587; mRS 0–2, 89.4% in the eMT group and 90.4%, p=0.890); also there was no significant difference regarding rates of parenchymal hemorrhage and mortality.

To evaluate the effect of eMT versus BMM/rMT on the outcome, all patients were entered in the PSM algorithm that generated 100 pairs balanced for age, pre-event mRS score, baseline NIHSS score, left-side stroke, occlusion of a dominant M2 division, and IVT. Univariate analysis on the matched cohort showed no significant difference between eMT and BMM/rMT on both excellent neurological outcome (85.0% in the eMT group and 76.0% in the BMM/rMT group, p=0.153) and functional independence (90.0% in the eMT group and 88.0% in the BMM/rMT group, p=0.821) (table 2). The distribution of mRS scores in the two matched cohorts is reported in online supplemental figure 2. Regarding safety issues, there was also no significant effect on the rate of intraparenchymal hemorrhage and 90-day mortality (table 2).

To address the issue of whether patients with LVO and mild symptoms subjected to eMT have better clinical outcome than those initially receiving BMM and eventually subjected to rMT after worsening,[7 10 12] the propensity score algorithm was used with the same set of covariates to match eMT patients with those receiving rMT and 59 new pairs were generated. Univariate analysis on the matched sample showed no significant difference of effect between eMT and rMT on both excellent neurological outcome (77.9% in the eMT group and 69.5% in the rMT group; p=0.403) and functional independence (86.4% in the eMT group and 78.0% in the rMT group; p=0.336) (table 2).

**Table 1** Demographics and baseline clinical, radiological, and procedural parameters of the raw population of patients

| | eMT (n=180) | BMM/rMT (n=208) | P value* |
|---|---|---|---|
| Gender (female), n (%) | 87 (48.3%) | 102 (49.0%) | 0.971 |
| Age, mean (±SD) | 70 (±13.9) | 70.2 (±11.9) | 0.701 |
| Atrial fibrillation, n (%) | 63 (35%) | 64 (30.8%) | 0.811 |
| Diabetes, n (%) | 34 (18.9%) | 39 (18.8%) | 0.329 |
| CAD, n (%) | 37 (20.6%) | 45 (21.6%) | 0.202 |
| Pre-event mRS score, median (IQR) | 0 (0–0) | 0 (0–1) | 0.998 |
| Baseline NIHSS score, median (IQR) | 4 (2–5) | 3 (2–5) | **<0.001** |
| ASPECT score, median (IQR) | 9 (9–10) | 9 (9–10) | 0.794 |
| Left-side stroke, n (%) | 110 (61.1%) | 127 (61.1%) | 1.000 |
| Dominant M2 division, n (%) | 120 (66.7%) | 108 (51.9%) | **0.005** |
| M2 branch, n (%) | | | 0.101 |
| Superior | 74 (41.1%) | 77 (37.0%) | |
| Middle | 34 (18.9%) | 25 (12.0%) | |
| Inferior | 72 (40.0%) | 106 (51.0%) | |
| IVT, n (%) | 54 (30.0%) | 133 (63.9%) | **<0.001** |
| mTICI 2b-3, n (%) | 155 (86.1%) | 78 (89.6%)† | 0.671 |
| 90-day mRS 0–1, n (%) | 146 (81.1%) | 163 (78.4%) | 0.587 |
| 90-day mRS 0–2, n (%) | 161 (89.4%) | 188 (90.4%) | 0.890 |
| IPH, n (%) | | | 0.185 |
| No IPH | 170 (94.4%) | 191 (92.0%) | |
| Type 1 IPH | 8 (4.5%) | 13 (6.1%) | |
| Type 2 IPH | 2 (1.1%) | 4 (1.9%) | |
| 90-day mortality, n (%) | 6 (3.3%) | 8 (3.8%) | 1.000 |

*Statistical significance was considered at $p<0.05$.
†87 patients of the BMM/rescue MT group were subjected to rescue mechanical thrombectomy.
ASPECT, Alberta Stroke Program Early CT; BMM, best medical management; CAD, coronary artery disease; eMT, early mechanical thrombectomy; IPH, intraparenchymal hemorrhage; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; mTICI, modified Treatment In Cerebral Infarction; n, number of patients; NIHSS, National Institutes of Health Stroke Scale; rMT, rescue mechanical thrombectomy.;

In order to identify possible predictors of clinical outcome in patients with a minor stroke and M2 occlusion that can be valuable when deciding the most appropriate type of treatment, baseline demographics and clinical, neuroradiological and procedural characteristics were compared between patients of the entire population (n=388) after division into two groups on the basis of their 90-day neurological outcome (mRS 0–1 vs mRS 2–6). In univariate analysis, lower baseline NIHSS score and involvement of the M2 inferior branch were associated with excellent neurological outcome, whereas a pre-event mRS score of 1 was associated with an unfavorable outcome (table 3). In multivariate analysis, involvement of the M2 inferior branch remained as the only independent predictor of excellent neurological outcome (OR 0.922, 95% CI 0.854 to 0.996, p=0.023), whereas a pre-event mRS score of 1 was an independent predictor of unfavorable outcome (OR 1.214, 95% CI 1.087 to 1.355, p=0.001) (figure 1). Baseline NIHSS score, involvement of a dominant M2 division, and the side of the stroke were not

**Table 2** Univariate analysis after propensity score matching

| Effect of eMT and BMM/rMT on clinical outcome | | | | |
|---|---|---|---|---|
| | eMT (n=100) | BMM/rMT (n=100) | Total (n=200) | P value * |
| mRS 0–1, n (%) | 85 (85.0%) | 76 (76.0%) | 161 (80.5%) | 0.153 |
| mRS 2–6, n (%) | 15 (15.0%) | 24 (24.0%) | 39 (19.5%) | |
| mRS 0–2, n (%) | 90 (90.0%) | 88 (88.0%) | 178 (89.0%) | 0.821 |
| mRS 3–6, n (%) | 10 (10.0%) | 12 (12.0%) | 22 (11.0%) | |
| **Effect of eMT and BMM/rMT on safety outcome measures** | | | | |
| | eMT (n=100) | BMM/rMT (n=100) | Total (n=200) | P value * |
| IPH | | | | 0.219 |
| No IPH, n (%) | 98 (98.0%) | 94 (94.0%) | 192 (96.0%) | |
| Type 1 IPH, n (%) | 1 (1.0%) | 4 (4.0%) | 5 (2.5%) | |
| Type 2 IPH, n (%) | 1 (1.0%) | 2 (2.0%) | 3 (1.5%) | |
| 90-day mortality, n (%) | 5 (5.0%) | 6 (6.0%) | 11 (5.5%) | 1.000 |
| **Effect of eMT and rMT on clinical outcome** | | | | |
| | eMT (n=59) | rMT (n=59) | Total (n=118) | P value * |
| mRS 0–1, n (%) | 46 (77.9%) | 41 (69.5%) | 87 (73.7%) | 0.403 |
| mRS 2–6, n (%) | 13 (22.1%) | 18 (30.5%) | 31 (26.3%) | |
| mRS 0–2, n (%) | 51 (86.4%) | 46 (78.0%) | 97 (82.2%) | 0.336 |
| mRS 3–6, n (%) | 8 (13.6%) | 13 (22.0%) | 21 (17.8%) | |

*Statistical significance was considered at p<0.05.
BMM, best medical management; eMT, early mechanical thrombectomy; IPH, intraparenchymal hemorrhage; mRS, modified Rankin Scale; n, number of patients; rMT, rescue mechanical thrombectomy.

**Table 3** Univariate analysis of baseline predicting factors for clinical outcome

| Variables | mRS 0–1 (n=309) | mRS 2–6 (n=79) | P value* |
|---|---|---|---|
| Gender (female), n (%) | 152 (49.2%) | 37 (46.8%) | 0.804 |
| Age, mean (±SD) | 69.2 (±13.2) | 73.7 (±11.8) | **0.005** |
| Atrial fibrillation, n (%) | 98 (31.7%) | 29 (36.7%) | 0.248 |
| Diabetes, n (%) | 57 (18.4%) | 16 (20.3%) | 0.670 |
| CAD, n (%) | 67 (21.7%) | 15 (19.0%) | 0.743 |
| Pre-event mRS score=1, n (%) | 85 (27.5%) | 28 (35.4%) | **<0.001** |
| Baseline NIHSS score, median (IQR) | 3 (2–5) | 4 (3–5) | **0.012** |
| ASPECT score, median (IQR) | 10 (9–10) | 9 (9–10) | 0.069 |
| Left-side stroke, n (%) | 192 (62.1%) | 45 (57.0%) | 0.476 |
| Dominant M2 division, n (%) | 172 (55.7%) | 50 (63.3%) | 0.431 |
| M2 branch, n (%) | | | **0.022** |
| Superior | 111 (35.9%) | 39 (49.3%) | |
| Middle | 47 (15.2%) | 11 (14.0%) | |
| Inferior | 151 (48.9%) | 29 (36.7%) | |
| IVT, n (%) | 153 (49.5%) | 34 (43.0%) | 0.367 |

*Statistical significance was considered at p<0.05.
ASPECT, Alberta Stroke Program Early CT; CAD, coronary artery disease; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; n, number of patients; NIHSS, National Institutes of Health Stroke Scale.

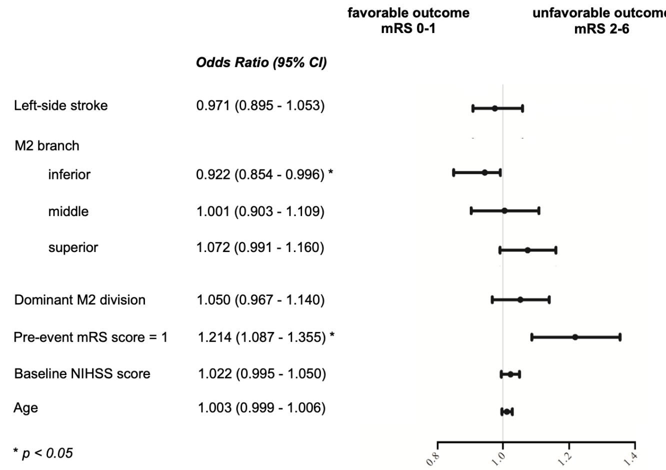


**Figure 1** Forest plot of baseline predictors of clinical outcome. mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

predictive. The goodness of fit for this logistic regression model was confirmed with the Hosmer-Lemeshow test (p=0.9456)

## DISCUSSION

Our multicenter retrospective analysis has shown no benefit of eMT in patients with isolated M2 occlusion and an NIHSS score ≤5 over a therapeutic approach based on BMM with the possibility of rMT in case of early neurological deterioration.

The appropriateness of MT in patients with LVO and minor symptoms is debated, particularly in distal occlusions. The data available on this subgroup of patients, deriving from retrospective studies and meta-analysis, are uneven and often contradictory. In the study by Goyal *et al* on patients with LVO and minor baseline symptoms, subgroup analysis showed a lower, although non-significant, rate of excellent outcome and a significant higher rate of asymptomatic intracranial hemorrhage in patients with M2 occlusion subjected to early MT compared with patients receiving BMM only.[9] Similarly, in the MINOR-STROKE collaboration study, intended bridging therapy with IVT followed by MT resulted in lower rates of excellent neurological outcome and functional independence and a higher rate of intracranial hemorrhage compared with IVT alone.[21] A more recent meta-analysis has shown that eMT in patients with M2 occlusion is associated with a lower chance of being free of disability (mRS 0–1) or having functional independence and higher rate of symptomatic hemorrhage compared with BMM. However, patients receiving rMT following END during BMM were excluded from this analysis, possibly resulting in a biased selection of medically managed patients with a mainly favorable clinical course.[22] Conversely, in a single center retrospective study that involved 169 consecutive patients admitted between 2005 and 2020, similar rates of favorable outcome were observed between patients receiving IVT only versus endovascular treatment (consisting of intra-arterial thrombolysis or MT) and between IVT only versus MT only. When patients treated after 2015 were analyzed separately, MT was associated with a significantly better shift of the 90-day mRS score compared with IVT only, possibly due to the introduction of last-generation thrombectomy devices.[23] Finally, a more recent analysis of three randomized controlled trials and two prospective non-randomized studies has shown no association between MT and better clinical outcome in patients with isolated M2 occlusion and minor or mild symptoms (baseline NIHSS below 6 or 10) in comparison with medical management.[24]

In our analysis, the proportion of minor stroke patients that achieved a favorable outcome regardless of the type of acute treatment was higher than what was reported in other studies on the effect of MT in M2 occlusions[3–6]; this difference mostly resides in the fact that the latter included patients with significantly higher baseline NIHSS scores. Indeed, the point that baseline NIHSS score is one of the main predictors of clinical outcome[1] should always be considered when defining the most appropriate treatment in patients with AIS due to LVO and minor deficits, particularly in the presence of a more peripheral occlusion of the MCA.

Although rMT performed after END is associated with higher odds of a favorable outcome,[7] still patients with minor symptoms receiving eMT have been reported to have a better clinical outcome compared with those receiving rMT after unsuccessful BMM. However, this has been shown in cohorts that included patients not only with isolated M2 occlusion but also with more proximal ones.[12 25] After accounting for the relatively low number of patients and a possible selection bias (ie, our rMT group may possibly represent the aggregation of patients having an unfavorable clinical course despite BMM), in our study we did not find a significant difference between eMT and rMT concerning clinical outcome. We believe that this aspect may represent a relevant issue when deciding the most appropriate type of acute treatment in these patients, together with the evidence that IVT is more effective in M2 occlusions rather than in proximal ones[26] and the link between reperfusion and good functional outcome may be less definite in the presence of a distal MCA involvement.[27]

In this uncertain scenario, baseline clinical and neuroradiological predictors of outcome can be valuable when deciding the most appropriate type of treatment. In our analysis we found a significant association between favorable neurological outcome and involvement of the M2 inferior branch. This appears in line with previous evidence that has shown that the involvement of the superior branch is associated with lower chances of achieving good neurological outcome compared with the inferior branch occlusion, because it provides blood supply to more eloquent brain areas.[28 29]

Overall, our results agree with the conclusions of recent studies[21 23] and underline the lack of benefit of early MT in patients with M2 occlusion and minor deficit compared with a more prudent approach. Therefore, we believe that in this subgroup of patients it is reasonable to consider best medical management, with IVT when possible, as the first option and to assess the possibility of MT on END or in the presence of involvement of the superior M2 branch. Also, additional neuroradiological criteria, such as the presence of a mismatch pattern in the CT perfusion study, may be helpful in orientating the more appropriate treatment in this subgroup of patients, as already suggested.[30]

Nonetheless, our results must be viewed with caution in consideration of the several limitations deriving from the retrospective observational design of the study. A significant bias may arise from the fact that the case-by-case decision on treatment was at the discretion of the managing physicians and/or based on the preferred therapeutic modality of each participating center—certainly outside the more rigid criteria defined in a clinical trial. In addition, although clinical records were carefully reviewed, the possibility of mistakes in data entry cannot be excluded in a minority of patients. Propensity score matching, applied in our study to minimize differences in baseline characteristics for treatment analysis, was centered on a set of covariates that we believe are important as predictors of clinical outcome, but it is possible that other relevant factors may have been overlooked. Also, these results come from a relatively large (and uniform as concerns the modality of endovascular treatment) collection of patients with minor stroke and isolated M2 occlusion receiving different acute treatments, in consideration of the rarity of the two conditions combined, but our sample size might still not be sufficient to detect significant differences.

It is expected that forthcoming randomized controlled trials will clarify the more appropriate acute treatment for AIS patients with single M2 occlusion and minor symptoms. However, given the high rate of favorable clinical outcome in this subgroup of patients despite the adopted type of treatment, a very large sample size will probably be needed to draw meaningful conclusions.

## CONCLUSIONS

The appropriateness of MT in patients with minor stroke due to isolated M2 occlusion is controversial. Our study has shown no benefit of eMT over BMM with the possibility of rMT in case of neurological worsening. Nonetheless, this issue remains open for clarification and the need for an unambiguous recommendation in clinical practice is urgent.

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**Contributors** AMA, FC, VB, IV, GDM and AB contributed to study concept or design, acquisition, analysis and interpretation of data and drafting/revision of the manuscript for content. GF, AP, LS, CR, CRo, AF, LM, MA, MP, AM, CC, MR, VDR, LB, GAL, MC, AAC, SLV, JDG, FCa, PP, LR, NL, FA, MPi, GB, DGR, FD, VS, NS, NB, MPG, ELo, AF, ELa, AC, RR and MB contributed to the acquisition, analysis and interpretation of data and revision of the manuscript for content. PC contributed to study concept or design and to drafting/revision of the manuscript for content. AB is the author acting as guarantor.

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## REFERENCES

1 Goyal M, Menon BK, van Zwam WH, *et al*. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387:1723–31.
2 Powers WJ, Rabinstein AA, Ackerson T, *et al*. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019;50:e344–418.
3 Sarraj A, Sangha N, Hussain MS, *et al*. Endovascular therapy for acute ischemic stroke with occlusion of the middle cerebral artery M2 segment. *JAMA Neurol* 2016;73:1291–6.
4 Saber H, Narayanan S, Palla M, *et al*. Mechanical thrombectomy for acute ischemic stroke with occlusion of the M2 segment of the middle cerebral artery: a meta-analysis. *J Neurointerv Surg* 2018;10:620–4.
5 Compagne KCJ, van der Sluijs PM, van den Wijngaard IR, *et al*. Endovascular treatment: the role of dominant caliber M2 segment occlusion in ischemic stroke. *Stroke* 2019;50:419–27.
6 Menon BK, Hill MD, Davalos A, *et al*. Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: meta-analysis of data from the HERMES collaboration. *J Neurointerv Surg* 2019;11:1065–9.
7 Kim J-T, Heo S-H, Yoon W, *et al*. Clinical outcomes of patients with acute minor stroke receiving rescue IA therapy following early neurological deterioration. *J Neurointerv Surg* 2016;8:461–5.
8 Pfaff J, Herweh C, Pham M, *et al*. Mechanical thrombectomy in patients with acute ischemic stroke and lower NIHSS scores: recanalization rates, periprocedural complications, and clinical outcome. *AJNR Am J Neuroradiol* 2016;37:2066–71.
9 Goyal N, Tsivgoulis G, Malhotra K, *et al*. Medical management vs mechanical thrombectomy for mild strokes: an international multicenter study and systematic review and meta-analysis. *JAMA Neurol* 2020;77:16–24.
10 Saleem Y, Nogueira RG, Rodrigues GM, *et al*. Acute neurological deterioration in large vessel occlusions and mild symptoms managed medically. *Stroke* 2020;51:1428–34.
11 Heldner MR, Jung S, Zubler C, *et al*. Outcome of patients with occlusions of the internal carotid artery or the main stem of the middle cerebral artery with NIHSS score of less than 5: comparison between thrombolysed and non-thrombolysed patients. *J Neurol Neurosurg Psychiatry* 2015;86:755–60.
12 Nagel S, Bouslama M, Krause LU, *et al*. Mechanical thrombectomy in patients with milder strokes and large vessel occlusions. *Stroke* 2018;49:2391–7.
13 Barber PA, Demchuk AM, Zhang J, *et al*. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. *Lancet* 2000;355:1670–4.
14 Goyal M, Menon BK, Krings T, *et al*. What constitutes the M1 segment of the middle cerebral artery? *J Neurointerv Surg* 2016;8:1273–7.
15 Capocci R, Shotar E, Sourour N-A, *et al*. Caution; confusion ahead…. *AJNR Am J Neuroradiol* 2017;38:E40–3.
16 Berge E, Whiteley W, Audebert H, *et al*. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J* 2021;6:I–LXII.
17 Gerber JC, Miaux YJ, von Kummer R. Scoring flow restoration in cerebral angiograms after endovascular revascularization in acute ischemic stroke patients. *Neuroradiology* 2015;57:227–40.
18 de Havenon A, Narata AP, Amelot A, *et al*. Benefit of endovascular thrombectomy for M2 middle cerebral artery occlusion in the ARISE II study. *J Neurointerv Surg* 2021;13:779–83.
19 von Kummer R, Broderick JP, Campbell BCV, *et al*. The Heidelberg bleeding classification: classification of bleeding events after ischemic stroke and reperfusion therapy. *Stroke* 2015;46:2981–6.
20 Austin PC. Some methods of propensity-score matching had superior performance to others: results of an empirical investigation and Monte Carlo simulations. *Biom J* 2009;51:171–84.
21 Seners P, Perrin C, Lapergue B, *et al*. Bridging therapy or IV thrombolysis in minor stroke with large vessel occlusion. *Ann Neurol* 2020;88:160–9.
22 Lin C-H, Saver JL, Ovbiagele B. Effects of endovascular therapy for mild stroke due to proximal or M2 occlusions: meta-analysis. *J Neurointerv Surg* 2023;15:350–5.
23 Dobrocky T, Piechowiak EI, Volbers B, *et al*. Treatment and outcome in stroke patients with acute M2 occlusion and minor neurological deficits. *Stroke* 2021;52:802–10.
24 Sarraj A, Parsons M, Bivard A, *et al*. Endovascular thrombectomy versus medical management in isolated M2 occlusions: pooled patient-level analysis from the EXTEND-IA trials, INSPIRE, and SELECT studies. *Ann Neurol* 2022;91:629–39.
25 Messer MP, Schönenberger S, Möhlenbruch MA, *et al*. Minor stroke syndromes in large-vessel occlusions: mechanical thrombectomy or thrombolysis only? *AJNR Am J Neuroradiol* 2017;38:1177–9.
26 del Zoppo GJ, Poeck K, Pessin MS, *et al*. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. *Ann Neurol* 1992;32:78–86.
27 Lemmens R, Christensen S, Straka M, *et al*. Patients with single distal MCA perfusion lesions have a high rate of good outcome with or without reperfusion. *Int J Stroke* 2014;9:156–9.
28 Seker F, Pfaff J, Neuberger U, *et al*. Comparison of superior and inferior division occlusions treated with endovascular thrombectomy. *Clin Neuroradiol* 2020;30:339–43.
29 Wang J, Qian J, Fan L, *et al*. Efficacy and safety of mechanical thrombectomy for M2 segment of middle cerebral artery: a systematic review and meta-analysis. *J Neurol* 2021;268:2346–54.
30 Gwak D-S, Kwon J-A, Shim D-H, *et al*. Perfusion and diffusion variables predict early neurological deterioration in minor stroke and large vessel occlusion. *J Stroke* 2021;23:61–8.