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M2 segment thrombectomy is not associated with increased complication risk compared to M1 segment: A meta-analysis of recent literature

Christopher Alexander, BS,* Andrew Caras, BS,* William Kyle Miller, MD,* Rizwan Tahir, MD,† Tarek R. Mansour, MD,† Azedine Medhkour, MD,* and Horia Marin, MD‡

Introduction: Recent clinical comparisons of M1 and M2 segment endovascular thrombectomy have reached incongruous results in rates of complication and functional outcomes. This study aims to clarify the controversy surrounding this rapidly advancing technique through literature review and meta-analysis.

Methods: A Pubmed search was performed (January 2015-September 2019) using the following keywords: “M2 AND ("stroke" OR "occlusion") AND ("thrombectomy" OR "endovascular")”. Safety and clinical outcomes were compared between segments via weighted Student’s t-test, Chi-square and odds ratio while study heterogeneity was analyzed using Cochran Q and I² tests.

Results: Pubmed identified 208 articles and eleven studies were included after full-text analysis, comprising 2,548 M1 and 758 M2 mechanical thrombectomy segment cases. Baseline National Institutes of Health Stroke Scale scores were comparatively lower in patients experiencing an M2 occlusion (16 ± 1.25 vs 13.6 ± 0.96, p < 0.01). Patients who underwent M2 mechanical thrombectomy were more likely to experience both good clinical outcomes (modified Rankin Scale 0/C0-2) (48.6% vs 43.5% respectively, OR 1.24; CI 1.05-1.47, p = 0.01) and excellent clinical outcomes (modified Rankin Scale 0-1) (34.7% vs. 26.5%, OR 1.6; CI 1.28-1.99, p < 0.01) at 90 days compared to M1 mechanical thrombectomy. Neither recanalization rates (75.3% vs 72.8%, OR 0.92, CI 0.75-1.13, p = 0.44) nor symptomatic intracranial hemorrhage rates (5.6% vs 4.9%, OR 0.92; CI 0.61-1.39, p= 0.7) were significantly different between M1 and M2 cohorts. Mortality was less frequent in the M2 cohort compared to M1 (16.3% vs 20.7%, OR 0.73; CI 0.57-0.94, p = 0.01). M1 and M2 cohorts did not differ in symptom onset-to-puncture (238.1 ± 46.7 vs 239.8 ± 43.9 min respectively, p=0.488) nor symptom onset-to-recanalization times (318.7 ± 46.6 vs 317.7 ± 71.1 min respectively, p = 0.772), though mean operative duration was shorter in the M2 cohort (61.8 ± 25.5 vs 54.6 ± 24 min, p < 0.01).

Conclusions: Patients who underwent M2 mechanical thrombectomy had a higher prevalence of good and excellent clinical outcomes compared to the M1 mechanical thrombectomy cohorts. Additionally, our data suggest lower mortality rates in the M2 cohort and symptomatic intracranial hemorrhage rates that are similar to the M1 cohort. Therefore, M2 segment thrombectomy likely does not pose a significantly elevated operative risk and may have a positive impact on patient outcomes.
Introduction

Numerous trials report safety and efficacy of mechanical thrombectomy (MT) for infants involving the M1 segment of the middle cerebral artery (MCA; extending from the terminal bifurcation of the internal carotid artery proximally to the main bifurcation distally) in comparison to intravenous thrombolytic therapy (e.g. alteplase) therapy alone.1–9 The Highly Effective Reperfusion Using Multiple Endovascular Devices (HERMES) meta-analysis of these early studies reported a number needed to treat of 2.6 for MT to reduce the modified Rankin Scale (mRS) by 1 point.6 However, while these studies excelled in demonstrating efficacy of MT for M1 and the internal carotid artery, they lacked sufficient statistical power for MT at the second middle cerebral artery segments (M2; extending from the bifurcation of the M1 segment proximally to the circular sulcus of the insula distally) and did not report distinct outcomes for the M2 MT cohorts. Thus, the American Heart Association (AHA) and American Stroke Association (ASA) 2018 guidelines for management of acute ischemic stroke strongly recommend mechanical thrombectomy M1 and ICA occlusions but only a weak, IIb, recommendation for M2 MT.7

Several institutional studies and meta-analyses have drawn contradictory conclusions since publication of the HERMES collaboration and AHA/ASA guidelines. M2 MT patients have reportedly experienced increased rates of symptomatic intracranial hemorrhage (sICH), even though incidence of good clinical outcomes (mRS of 0–2) between cohorts may not significantly differ.9 Timing parameters involving symptom onset-to-recanalization, symptom onset-to groin puncture, and operation duration are key variables for stroke treatment but have been rarely compared between M1 and M2 cohorts. One meta-analysis, published in 2018, examined the difference in stroke onset to recanalization time and reported no significant difference between segments.8 To our knowledge, no meta-analysis has examined the differences between operation time or symptom onset to groin puncture between M1 and M2 cohorts.

Several studies have thoroughly compared M1 and M2 MT since publication of the most recent meta-analysis by Kim et al.10–15 These studies may reflect current technology and increased operator familiarity with more distal MT procedures. Thus, a new meta-analysis is warranted to assess patient safety and outcome between M1 and M2 cohorts. sICH and mortality rates between cohorts may indicate the safety of this procedure while a more thorough analysis of operation durations may reflect the operator’s comfort and intraoperative complications when traversing the M2 segment. Clarifying these treatment aspects may help standardize and optimize M2 MT.

Methods

Literature Search

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.16 The PubMed database was queried with the terms “M2 AND (“stroke” OR “occlusion”) AND (“thrombectomy” OR “endovascular”)” from January 2015 to September 2019 to reflect the current state of the field. Studies were systematically screened against inclusion criteria by title and abstract. Studies were included if: (1) At least 10 patients with M2 vessel occlusion were treated with MT; (2) Separate M1 and M2 cohorts were included for comparison; and; (3) The patients underwent MT with non-Mechanical Embolus Removal in Cerebral Ischemia (MERCI) devices. MERCI devices were excluded to reflect the current state of technology in the field. Studies were excluded if they did not have ≥10 patients in congruence with other meta-analyses of MT.12,15 Case reports, meta-analyses, and literature reviews were also excluded. Titles and abstracts initially meeting inclusion criteria were more thoroughly screened via full-text analysis.

Data Extraction

Patient demographics (age and sex), baseline information (National Institutes of Health Stroke Score [NIHSS] at presentation and presence of left-sided stroke), medical comorbidities (atrial fibrillation, hypertension, and diabetes mellitus), and treatment aspects (administration of intravenous [IV] thrombolytic therapy, onset-to-puncture, onset-to-recanalization and operation duration time) were extracted from eligible papers. Clinical outcomes included successful recanalization rate as measured by a Thrombolysis in Cerebral Infarction (TICI) score of at least 2b/3, and either good (mRS score = 0–2) or excellent (mRS score = 0–1) functional outcomes 90 days post-intervention, sICH rates, and 90-day mortality.

Statistical Analysis

Extracted data was analyzed utilizing SPSS version 24 (IBM Corporation, Armonk, NY, USA) and Review Manager (RevMan) Version 5.3 (Nordic Cochrane Centre, The Cochrane Collaboration, 2014, Copenhagen, Denmark). Student’s t-tests were used for continuous data and Chi-
square was used for ordinal data. Odds ratios were used to compare outcome between cohorts. Alpha was set to 0.05. Cochran Q test and I² test were conducted to detect heterogeneity with significant heterogeneity defined as an I² value greater than 50%. The Mantel-Haenszel fixed-effect method was used for meta-analysis unless significant heterogeneity was discovered. Means were estimated from medians when possible by utilizing the formula developed by Wan et al. (15).

Results

Our search returned 208 studies from January 2015 to September 2019, of which 129 underwent full-text review (Fig. 1). Six studies were excluded for using older MERCI-type devices. Thirty-two studies were excluded as case reports, meta-analyses, or reviews. Twenty studies did not have enough patients (<10) and 60 studies did not separate their M1 and M2 cohorts. Notably, none of the five HERMES studies were included in this meta-analysis due to a lack of distinct outcomes data for the M2 MT cohorts. Ultimately, 11 studies were included comparing M1 patients (n = 2,548) to M2 patients (n = 758) (Table 1). Demographics, comorbidities, treatment timing and clinical outcomes between cohorts are compared below.

Demographics, Baseline Information and Medical Comorbidities

Table 2, presents demographic and baseline information. There was no difference in mean age between M1 and M2 cohorts (70.1 ± 2.2 vs 70.2 ± 2.5 years respectively, p = 0.507). Patients with M2 occlusion were 1.35 times more likely to receive IV thrombolytic therapy (63.4% vs 66.4%, OR 1.35;
95% CI 1.09–1.67, \( p < 0.01 \). Baseline NIHSS scores were comparatively lower in patients experiencing an M2 occlusion (16 ± 1.25 vs 13.6 ± 0.96, \( p < 0.01 \)). Patients were more likely to be male in the M2 cohort compared to M1 (49.2% vs 54.3%, OR 1.24; 95% CI 1.04–1.48, \( p = 0.02 \), \( I^2 = 46\% \)). There was no significant difference in prevalence of left-sided occlusion between M1 and M2 cohorts (49.3% vs 55.9% respectively, OR 1.21, 95% CI 0.96–1.53, \( p = 0.1 \)). Prevalence of hypertension, atrial fibrillation, and diabetes mellitus did not differ between cohorts (Table 2).

### Treatment Timing

Table 3 compares treatment timing between groups. M1 and M2 occlusions experienced similar symptom onset-to-puncture (238.1 ± 46.7 vs 239.8 ± 43.9 min respectively, \( p = 0.488 \)) and onset-to-recanalization times (318.7 ± 46.6 vs 317.7 ± 71.1 min respectively, \( p = 0.772 \)). M2 segment MT operative duration was significantly shorter than the M1 cohort (54.6 ± 24 vs. 61.8 ± 25.5 min respectively, \( p < 0.01 \)).

### Complications and Functional Outcome

M1 and M2 MT populations experienced similar sICH rates (5.6% vs 4.9% respectively, OR 0.92; 95% CI 0.61–1.39, \( p = 0.7 \)) (Fig. 2). The M2 MT cohort had a comparatively lower rate of mortality at 90 days (20.7% vs 16.3%, OR 0.73; 95% CI 0.57–0.94, \( p = 0.01 \)) (Fig. 3). Patients who underwent M2 MT were 1.24 times more likely to experience a good clinical outcome (mRS score = 0–2) (48.6% vs 43.5%, OR 1.24; 95% CI 1.05–1.47, \( p = 0.01 \), \( I^2 = 40\% \)) (Fig. 4a) and 1.60 times more likely to experience an excellent clinical outcome (mRS score of 0–1) (34.7% vs 26.5%, \( p < 0.01 \), \( I^2 = 48\% \)) at 90 days compared to the M1 MT cohort (Fig. 4b). Recanalization rates did not significantly differ between the M1 and M2 MT groups (75.3% vs 72.8% respectively, OR 0.92, CI 0.75–1.13, \( p = 0.44 \), \( I^2 = 27\% \)).

### Discussion

The 2018 AHA/ASA guidelines for management of acute ischemic strokes provides a weak, Ib, recommendation for endovascular treatment of M2 segment occlusions.\(^7\) Rai et al.\(^7\) estimated the national prevalence of M2 segment occlusions at 21,176 per year. Thus, our meta-analysis applies to a large population with a heretofore unclear treatment algorithm.

### Demographics, Baseline Information and Medical Comorbidities

Demographics were largely similar between the M1 and M2 cohorts except for a higher percentage of men treated for M2 occlusions compared to M1 occlusions. This has been unreported in previous meta-analyses. Given that the M1 cohort did not demonstrate differences

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**Table 1. Demographics and study information.** Means given ± standard deviation or [95% confidence interval] depending on statistics in cited study.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of cases</th>
<th>Device</th>
<th>Age (years)</th>
<th>Sex (male)</th>
<th>Left-sided Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alawieh et al. (19)</td>
<td>205</td>
<td>Aspiration or Stent Retriever</td>
<td>67.4 ± 16</td>
<td>67%</td>
<td>57.8%</td>
</tr>
<tr>
<td>Bhogal et al. (20)</td>
<td>479</td>
<td>Stent Retriever</td>
<td>72 ± 12.8</td>
<td>44.0%</td>
<td>47.0%</td>
</tr>
<tr>
<td>Compagne et al. (21)</td>
<td>759</td>
<td>Aspiration or Stent Retriever</td>
<td>70 ± 60–79</td>
<td>53.0%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Conte et al. (22)</td>
<td>244</td>
<td>Aspiration or Stent Retriever</td>
<td>67 ± 13</td>
<td>43.0%</td>
<td>47.0%</td>
</tr>
<tr>
<td>Dorn et al. (23)</td>
<td>104</td>
<td>Aspiration or Stent Retriever</td>
<td>69 ± 14</td>
<td>57.8%</td>
<td>61.6%</td>
</tr>
<tr>
<td>Goebel et al. (24)</td>
<td>137</td>
<td>Aspiration or Stent Retriever</td>
<td>NR</td>
<td>55.1%</td>
<td>48.7%</td>
</tr>
<tr>
<td>Kastrup et al. (25)</td>
<td>134</td>
<td>Stent Retriever</td>
<td>NR</td>
<td>62.7%</td>
<td>68.0%</td>
</tr>
<tr>
<td>Millan et al. (26)</td>
<td>122</td>
<td>Stent Retriever</td>
<td>NR</td>
<td>64.4%</td>
<td>51.6%</td>
</tr>
<tr>
<td>Nakano et al. (27)</td>
<td>187</td>
<td>Aspiration or Stent Retriever</td>
<td>76 ± 60–82</td>
<td>63.5%</td>
<td>43.8%</td>
</tr>
<tr>
<td>Protto et al. (28)</td>
<td>46</td>
<td>Stent Retriever</td>
<td>NR</td>
<td>70.2 ± 15.3</td>
<td>69.6 ± 13.2</td>
</tr>
<tr>
<td>Salahuddin et al. (29)</td>
<td>153</td>
<td>Aspiration or Stent Retriever</td>
<td>NR</td>
<td>59</td>
<td>59</td>
</tr>
</tbody>
</table>

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### Table 2. Baseline demographics and pre-existing conditions. Mean values ± standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>M1 (n/total)</th>
<th>M2 (n/total)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Baseline NIHSS</td>
<td>16 ± 1.25</td>
<td>13.6 ± 0.96</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Received intravenous thrombolytic therapy</td>
<td>63.4% (1149/1813)</td>
<td>66.4% (390/587)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean age</td>
<td>70.1 ± 2.2</td>
<td>70.0 ± 2.5</td>
<td>0.51</td>
</tr>
<tr>
<td>Male</td>
<td>49.2% (1010/2051)</td>
<td>54.3% (355/654)</td>
<td>0.02</td>
</tr>
<tr>
<td>Left-sided occlusion</td>
<td>49.3% (614/1246)</td>
<td>55.9% (217/388)</td>
<td>0.1</td>
</tr>
<tr>
<td>Medical comorbidity</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>38.3% (785/2051)</td>
<td>33.6% (220/654)</td>
<td>0.17</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>20.1% (413/2051)</td>
<td>21.4% (140/654)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62.7% (1285/2051)</td>
<td>65.4% (428/654)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

### Table 3. Procedure times and outcomes. Mean values ± standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>M1 (n/total)</th>
<th>M2 (n/total)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mean onset-to-puncture (min)</td>
<td>238.1 ± 46.7</td>
<td>239.8 ± 43.9</td>
<td>0.488</td>
</tr>
<tr>
<td>Mean onset-to-recanalization (min)</td>
<td>318.7 ± 46.6</td>
<td>317.7 ± 71.1</td>
<td>0.772</td>
</tr>
<tr>
<td>Mean operation time (min)</td>
<td>61.8 ± 25.5</td>
<td>54.6 ± 24.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Good clinical outcome (mRS 0–2) at 90 days</td>
<td>43.5% (996/2289)</td>
<td>48.6% (348/716)</td>
<td>0.01</td>
</tr>
<tr>
<td>Excellent clinical outcome (mRS 0–1) at 90 days</td>
<td>26.5% (475/1790)</td>
<td>34.4% (172/496)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TICI 2b/3</td>
<td>75.3% (1765/2343)</td>
<td>72.8% (463/636)</td>
<td>0.44</td>
</tr>
<tr>
<td>Complications</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>sICH</td>
<td>5.6% (118/2109)</td>
<td>4.9% (32/647)</td>
<td>0.7</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>20.7% (431/2087)</td>
<td>16.3% (93/571)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Fig. 2.** Forest plot of symptomatic intracranial hemorrhage (sICH) rates in M1 versus M2 mechanical thrombectomies.

**Fig. 3.** Forest plot of 90-day mortality rates in M1 versus M2 mechanical thrombectomies.
between sex, and that stroke is generally more common in women, this correlation potentially suggests etiological differences that should be examined in the future.\textsuperscript{18} The 2014 AHA/ASA guidelines for prevention of stroke in women list pregnancy, oral contraceptives, postmenopausal hormone replacement and atrial fibrillation as more common in women, thus increasing the likelihood of emboli.\textsuperscript{19,20} Proximal vessel and distal vessel occlusion are typically associated with distant emboli and local plaque rupture, respectively; however, distal occlusion may also result from smaller emboli.\textsuperscript{21} Men have a 9% larger mean MCA diameter which theoretically allows emboli to travel further distally.\textsuperscript{22} Additionally, estrogen has numerous inhibitory effects on atherosclerotic plaque progression.\textsuperscript{20} Thus, males theoretically have a higher ratio of local plaque ruptures to emboli.\textsuperscript{22} Evidence suggests cardioembolic disease causes more strokes in women, but sex differences in systemic embolization remain underreported.\textsuperscript{23} Further explanation of sex-based etiological differences is out of the scope of this article; however, Haast et al.\textsuperscript{20} provide excellent in-depth explanations on the subject.

We report a significantly lower baseline NIHSS score in the M2 population which may inherently contribute to better clinical outcomes in M2 MT. Baseline NIHSS scores do correlate with favorable outcomes.\textsuperscript{24} However, Reznik et al.\textsuperscript{25} argue that baseline NIHSS score is a less accurate predictor of outcomes compared to both 24-hour and discharge NIHSS scores, which are both currently underreported in the literature. Smith et al.\textsuperscript{26} report mean baseline NIHSS scores of 13.4 and 11.5 in respective M1 and M2 cohorts receiving medical management (but not endovascular therapy). Additionally, M2 patients experienced “good” clinical outcomes more frequently (40% vs. 34%) but equal mortality rates (40%). Thus, baseline NIHSS score may not accurately predict mortality between M1 and M2 cohorts.

IV. Thrombolytic Therapy and sICH Rates

To our knowledge, this is the first meta-analysis to report comparatively higher odds of receiving IV thrombolytic therapy (e.g. recombinant tPA) in M2 patients. This finding may intuitively stem from a lack of clear treatment guidelines; patients may be offered tPA within the treatment window, then receive subsequent thrombectomy if symptoms do not improve. Raychev et al.\textsuperscript{27} recently reported an increased risk of parenchymal hematomas in patients treated with IV tPA, theoretically conferring increased risk to our M2 cohort compared to M1. However, we do not report any significant differences in sICH between cohorts. This finding may result from smaller hematomas originating from the M2 segment that do not result in clinically significant symptoms. Cappellari et al.\textsuperscript{28} recently identified patient age, NIHSS score at presentation, onset-to-recanalization time, recanalization rate, and Alberta Stroke Program Early CT (ASPECT) score as predictors of sICH in patients undergoing endovascular procedures. They did not examine the effect of infarct location on sICH rates, but our data suggest it may be negligible between M1 and M2 segments.
**Treatment Timing**

Hassan et al.\(^29\) recently reported that longer symptom onset-to-groin puncture and groin puncture-to-recanalization are both predictors of unfavorable outcomes (mRS = 3–6) at 90 days (11). Similarly, lower procedure times correlated with higher rates of favorable outcomes. Our cohorts did not significantly differ in symptom onset-to-puncture nor symptom onset-to-recanalization timing, but this may be due to relatively low statistical power for these variables. However, we report significantly shorter procedure duration in the M2 cohort compared to the M1 cohort by 7.2 min. This difference is likely clinically significant in salvaging the ischemic penumbra.\(^30,31\) Although the penumbra resulting from an M2 occlusion can be relatively small, the role of penumbra size and relation to post-interventional outcome (e.g. TICI score) between proximal and distal occlusion cohorts should be further investigated.\(^32\) Moreover, Hassan et al.\(^29\) associate improved outcomes with procedures ≤ 60 min duration, which applies to our M2 cohort; additionally, they argue that thrombus size may impact occlusion location with proximal segments conferring a higher probability of containing large, difficult to remove thrombi.

**Clinical Outcome and Mortality**

Kim et al.\(^15\) and Saber et al.\(^15\) observed comparatively higher odds of good clinical outcomes in M2 MT after 90 days; conversely, Salahuddin et al.\(^9\) describe no significant difference in rates of good and excellent clinical outcomes between segments. We report higher rates of both good and excellent clinical outcomes in the M2 cohort at 90 days which is likely influenced by its comparatively smaller vascular territory. Interestingly, analyses by Kim et al.\(^15\) and Saber et al.\(^8\) were published later than one by Salahuddin et al.\(^9\) This may suggest improved M2 recanalization safety over time due to improved technology and provider familiarity. Sarraj et al. report that endovascular therapy (MT or intra-arterial thrombolytics) in the M2 segment imparted a 3.2 times greater odds of good clinical outcomes compared with medical management.\(^33\) Overall, comparison of our results with medical management suggests M2 MT demonstrates comparatively increased efficacy.\(^26,33\) Our inclusion of new clinical studies and exclusion of old technologies (MERCI devices) likely improved good and excellent clinical outcome rates. We expect continual improvement for M2 MT, compared to both M1 MT and M2 thrombolytic therapy.

Previous meta-analyses vary in reported mortality rates. Kim et al.\(^15\) and Salahuddin et al.\(^9\) reported no significant difference, whereas Saber et al.\(^8\) report significantly increased mortality in the M2 population. In contrast, our meta-analysis suggests significantly decreased 90-day mortality in the M2 population which may be influenced by our lower sICH rates compared to previous meta-analyses. Our findings may suggest that M2 MT decreases 90-day mortality rates compared to medical management alone, as medical management of M1 and M2 occlusions have produced similar mortality rates.\(^26\) This hypothesis requires more data from well-designed studies.

**Thrombectomy Devices**

We included studies that utilized both aspiration and stent retriever devices but did not study each separately as subgroups. Future research in this field should emphasize potential outcome benefits between these devices. To our knowledge, previous meta-analyses did not exclude MERCI devices. Recent studies have demonstrated superiority of newer stent retrievers over older MERCI devices.\(^34\) Therefore, we chose to exclude MERCI devices to reflect current practices. Stent retriever covers prevent distal embolization during thrombus removal and may in turn improve recanalization rates.\(^35\) These technical improvements likely contribute to our lower sICH and mortality rates, and improved clinical outcomes, in the M2 MT cohort compared to previous meta-analyses.\(^9,12\) Thus, due to rapid technological advancements in this field, we advocate for relatively frequent or at least updated meta-analyses.

**Limitations**

The retrospective nature of many of the included studies introduce confounding variables that may be mitigated by appropriate prospective study designs. Different treatment protocols and selection criteria could be minimized by stringently limiting inclusion criteria; however, this would secondarily limit statistical power for several variables. Conversely, several variables of interest were insufficiently reported for meaningful analysis, including NIHSS at discharge and non-significant intracranial hemorrhage rates. Although most studies clearly defined the M2 segment (whether anatomically or functionally), heterogeneity or overt omission of this definition in some studies slightly limits the external validity of our findings.

We feel our data adequately demonstrates the safety of M2 MT. An inability to stratify individual patients based on NIHSS, infarct location (beyond M1 and M2 segments), and perhaps a control group of patients receiving medical management alone, precluded our ability to compare efficacy within this meta-analysis. Controlling for these variables would be extremely difficult; although not impossible, prospective studies would have numerous ethical considerations and may slow treatment times. Retrospective studies would require extensive multivariate analysis based on patient demographics, infarct location, and individual anatomical variations.

Finally, an inherent selection bias may exist between M2 infarcts treated with MT and those treated with thrombolytic therapy. Experienced providers may feel more comfortable in attempting M2 MT as an initial treatment modality. Additionally, patients with proximal M2 infarcts may be more likely to receive MT compared with...
distal M2 infarcts. Few studies describe specific location of thrombus within the M2 segment, impeding correlations between location and outcome.

Conclusions
This study was designed to clarify the safety of M2 MT and examine clinical outcomes. Both good and excellent clinical outcomes were more prevalent for M2 MT compared to the M1 MT population. M2 MT was associated with a comparatively decreased 90-day mortality rate despite no significant difference in sICH incidence. In contrast to previous meta-analyses, our data suggest that M2 MT is becoming safer, possibly due to technological advancements and increased provider experience and familiarity with the procedure. M2 MT likely does not confer significantly higher operative risk compared to the M1 segment and may improve clinical outcomes.

References


