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# Incidence and clinical outcomes of perforations during mechanical thrombectomy for medium vessel occlusion in acute ischemic stroke: A retrospective, multicenter, and multinational study

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**Abstract**

**Background:** Mechanical thrombectomy (MT) has revolutionized the treatment of acute ischemic stroke (AIS) due to large vessel occlusion (LVO), but its efficacy and safety in medium vessel occlusion (MeVO) remain less explored. This multicenter, retrospective study aims to investigate the incidence and clinical outcomes of vessel perforations (confirmed by extravasation during an angiographic series) during MT for AIS caused by MeVO.

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**Methods:** Data were collected from 37 academic centers across North America, Asia, and Europe between September 2017 and July 2021. A total of 1373 AIS patients with MeVO underwent MT. Baseline characteristics, procedural details, and clinical outcomes were analyzed.

**Results:** The incidence of vessel perforation was 4.8% (66/1373). Notably, our analysis indicates variations in perforation rates across different arterial segments: 8.9% in M3 segments, 4.3% in M2 segments, and 8.3% in A2 segments ( $p=0.612$ ). Patients with perforation had significantly worse outcomes, with lower rates of favorable angiographic outcomes (TICI 2c-3: 23% vs 58.9%,  $p<0.001$ ; TICI 2b-3: 56.5% vs 88.3%,  $p<0.001$ ). Functional outcomes were also worse in the perforation group (mRS 0–1 at 3 months: 22.7% vs 36.6%,  $p=0.031$ ; mRS 0–2 at 3 months: 28.8% vs 53.9%,  $p<0.001$ ). Mortality was higher in the perforation group (30.3% vs 16.8%,  $p=0.008$ ).

**Conclusion:** This study reveals that while the occurrence of vessel perforation in MT for AIS due to MeVO is relatively rare, it is associated with poor functional outcomes and higher mortality. The findings highlight the need for increased caution and specialized training in performing MT for MeVO. Further prospective research is required for risk mitigation strategies.

## Keywords

Stroke, AIS, MeVo, perforation, mechanical thrombectomy, MT

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## Introduction

The transformative impact of mechanical thrombectomy (MT) on the management of acute ischemic stroke (AIS) patients with large vessel occlusion (LVO) has been well established.<sup>1</sup> As early as 2015, a series of five randomized clinical trials shed light on the significant advantages of MT over traditional treatment methods for LVO.<sup>2</sup> Since these seminal findings, the scope for MT indications has been continuously broadening.<sup>1,2</sup> However, a noticeable gap exists in the literature regarding the efficacy of MT in AIS caused by medium vessel occlusion (MeVO).

Several ongoing randomized trials, such as DISTAL (Endovascular Therapy Plus Best Medical Treatment (BMT) vs BMT Alone for Medium Vessel Occlusion sTroke, ClinicalTrials.gov Identifier: NCT05029414), DISTALS (Distal Ischemic Stroke Treatment With Adjustable Low-profile Stentriever, NCT05152524), DISCOUNT (Evaluation of Mechanical Thrombectomy in Acute Ischemic Stroke Related to a Distal Arterial Occlusion, NCT05030142), ESCAPE-MEVO (Endovascular Treatment to improve outcomes for Medium Vessel Occlusions, NCT05151172), and FRONTIER-AP (Randomized controlled trial of the clinical outcome and safety of endovascular vs standard medical therapy for stroke with medium sized vessel occlusion),<sup>3</sup> aim to evaluate the benefit of MT in MeVO. Critics argue that MT's effectiveness in MeVO may be compromised due to potential challenges like thinner vessel walls, increased vessel tortuosity, and the absence of specialized devices tailored for medium-sized vessels.<sup>4,5</sup> These factors could increase the risk of complications such as hemorrhage, thereby reducing the procedure's net clinical benefit.

One serious complication of MT is vessel perforation, which is often linked to poor functional outcomes including death.<sup>6</sup> Despite its clinical significance, data on

perforation during MT is limited, particularly in the context of MeVO.<sup>7</sup> In cases involving medium-sized vessels, the dynamics of perforation might differ from those in large vessels. For example, the rate of blood flow during active extravasation might be slower, and the affected brain volume could be smaller if vessel occlusion is required to stop extravasation.<sup>8</sup>

Therefore, this study sought to contribute to the evolving landscape by focusing on the incidence and outcomes of perforations during MT in AIS patients with MeVO. By doing so, we hope to provide clinicians with valuable insights that can guide treatment decisions for this specific, yet understudied, patient population.

## Methods

The study received approval from the local ethical standards committee at each participating site, and informed consent from patients was waived. The data supporting this study's findings are available from the corresponding author upon reasonable request.

### Setting and ethical approval

Characteristics and outcomes of patients with acute ischemic stroke due to medium vessel occlusions (MeVO) treated with MT or MT + IVtPA were collected at 37 academic centers in North America, Asia, and Europe. Data were collected between September 2017 and July 2021. Data for this study were collected prospectively and reviewed retrospectively. Institutional review board approval was obtained at each individual participating center. The local board-certified neurointerventionalist reviewed all cases before sending their data to the MAD MT consortium. They determined the angiographic treatment success before the

data was sent to the consortium, which was self-reported by each center.

### Data collection and outcomes

Baseline characteristics were recorded for patients. Baseline characteristics and risk factors of interest included sex (male or female), age, hypertension, hypercholesterolemia, diabetes mellitus, atrial fibrillation, and smoking status. Pre-morbid modified Rankin Scale (mRS) score and occlusion vessel were similarly recorded. The onset of stroke was trichotomized into witnessed, unknown, or wake-up stroke. NIHSS was recorded at the presentation. Baseline Alberta Stroke Program Early CT Score (ASPECTS) was collected per each institution's protocol.

Procedural details of interest included antiplatelet and anticoagulation medication status, mothership versus drip-and-ship, time from onset to puncture and recanalization, vital sign readings (blood pressure, temperature, heart rate), glycemic readings, anesthesia type (general, sedation, or local), access site (femoral or radial), heparin administration, and imaging after MT (computed tomography (CT), magnetic resonance (MR), or none).

The primary outcome of interest was a good functional outcome defined as an mRS score of 0–2 measured at 90 days. Secondary outcomes of interest included first-pass effect (FPE) thrombolysis in cerebral infarction (TICI) scores, number of thrombectomy passes, and mRS scores at 90 days. mRS and TICI scores were adjudicated as per each institution's protocol.

### Procedural and technical details

Treatment consisted of MT alone or MT+ intravenous (IV) tissue plasminogen activator (tPA), (IVtPA). MT access site, either femoral artery or radial artery, was left to the individual operator's discretion. Similarly, the number of passes was left to the treating physician's discretion and institutional guidelines. Additionally, the operator determined the MT device selection and type (aspiration or stent-retriever).

### Definitions

MVs were defined to encompass codominant or nondominant M2-segments, M3- and M4-segments of the MCA as well as the anterior cerebral artery (ACA) and posterior cerebral artery (PCA) and their branches, respectively.<sup>4</sup> MeVO was defined as occlusion of one or several of the above mentioned MVs. Perforation was confirmed by extravasation during an angiographic series.

### Statistical analysis

Categorical variables were summarized as frequencies with percentages and compared using the Chi-square test.

Continuous variables were summarized as medians with interquartile ranges (IQR) and compared using the Mann-Whitney *U* test. To address missing data, we employed the multiple imputation method with 10 imputations, ensuring robustness in our analysis. All statistical analyses were performed using R Studio version 4.2.2. For all statistical tests within the results synthesis, a *p* value of  $\leq 0.05$  was used to indicate statistical significance.

## Results

### Baseline characteristics

The study encompassed 1373 AIS patients with MeVOs, of whom 66 (4.8%) incurred vessel perforation during MT. A detailed analysis revealed variations in perforation rates across different arterial segments: M3 segments showed a perforation rate of 8.9% (14/146), compared to 4.3% in M2 segments (46/1075), and 8.3% in A2 segments (3/36) ( $p=0.612$ ). The demographic and clinical characteristics were comparable across patients with and without perforations (Table 1). The median age for the cohort was 64 years (IQR: 47–79), with no statistically significant difference between perforation and non-perforation groups ( $p=0.496$ ). Sex distribution was balanced between the two groups, with 50.4% females in non-perforation group and 57.6% in the perforation group ( $p=0.313$ ). Pre-existing comorbidities such as hypertension ( $p=0.622$ ), hypercholesterolemia ( $p=0.4$ ), and atrial fibrillation ( $p=0.36$ ) did not show a statistically significant association with the incidence of perforation. Initial stroke severity, assessed via NIHSS and ASPECTS, was also comparable ( $p=0.337$  and  $p=0.463$ , respectively).

### Procedural Details

Various MT techniques were employed, including stent retrievers, aspiration, or a combination of both. The first-line technique had no significant influence on perforation incidence ( $p=0.083$ ). Pre-operative vital signs indicated a slight but significant elevation in systolic (157.5 (IQR: 143.5–180) vs 150 (IQR: 131.8–167),  $p=0.012$ ) and diastolic blood pressure (90 (IQR: 80–100) vs 83 (IQR: 74–95),  $p=0.013$ ) in the perforation group compared to non-perforation group. However, the two groups' other procedural parameters, like time delays from stroke onset to arterial puncture and recanalization, were statistically similar (Table 2).

### Outcomes

Angiographic and clinical outcomes differed significantly between the two groups. TICI scores of 2c-3 and 2b-3 were significantly less likely in the perforation group compared to the non-perforation group (14/66, 23% vs 757/1307, 58.9%;  $p < 0.001$  and 35/66, 56.5% vs

**Table 1.** Baseline characteristics of the included patients in the study.

Variable	No perforation	Perforation	Total	p Value
Sex				
Female	659 (50.4)	38 (57.6)	697 (50.8)	0.313
Male	648 (49.6)	28 (42.4)	676 (49.2)	
Age*	64.0 (47.0 to 79.0)	64.0 (50.2–84.2)	64.0 (47.0 to 79.0)	0.496
Hypertension	923 (70.6)	49 (74.2)	972 (70.8)	0.622
Cholesterol	473 (36.2)	20 (30.3)	493 (35.9)	0.4
Initial occlusion				
A1	3 (0.2)	0 (0.0)	3 (0.2)	0.612
A2	33 (2.5)	3 (4.5)	36 (2.6)	
A3	9 (0.7)	0 (0.0)	9 (0.7)	
ACA	1 (0.1)	0 (0.0)	1 (0.1)	
AICA	1 (0.1)	0 (0.0)	1 (0.1)	
M2	1029 (78.7)	46 (69.7)	1075 (78.3)	
M3	146 (11.2)	14 (21.2)	160 (11.7)	
M4	13 (1.0)	1 (1.5)	14 (1.0)	
P1	32 (2.4)	2 (3.0)	34 (2.5)	
P2	36 (2.8)	0 (0.0)	36 (2.6)	
P3	1 (0.1)	0 (0.0)	1 (0.1)	
PICA	2 (0.2)	0 (0.0)	2 (0.1)	
SCA	1 (0.1)	0 (0.0)	1 (0.1)	
Location				
Anterior	1234 (94.4)	64 (97.0)	1298 (94.5)	0.539
Posterior	73 (5.6)	2 (3.0)	75 (5.5)	
Diabetes mellitus (DM)	302 (23.1)	10 (15.2)	312 (22.7)	0.176
Atrial fibrillation (Afib)	479 (36.6)	20 (30.3)	499 (36.3)	0.36
Smoking	172 (13.2)	5 (7.6)	177 (12.9)	0.257
Antiplatelet use prior to EVT	363 (31.2)	23 (39.0)	386 (31.5)	0.263
Anticoagulation use prior to EVT	269 (24.1)	12 (20.3)	281 (23.9)	0.619
mRS before stroke				
0	804 (64.7)	40 (64.5)	844 (64.7)	0.837
1	175 (14.1)	8 (12.9)	183 (14.0)	
2	127 (10.2)	7 (11.3)	134 (10.3)	
3	102 (8.2)	6 (9.7)	108 (8.3)	
4	35 (2.8)	1 (1.6)	36 (2.8)	
5	0 (0.0)	0 (0.0)	0 (0.0)	
Baseline NIHSS*	11.0 (6.0–17.0)	13.0 (7.0–18.0)	11.0 (6.0–17.0)	0.337
ASPECTS*	6.0 (5.0–7.0)	6.0 (4.5–7.0)	6.0 (5.0–7.0)	0.463
Occlusion				
Distal	241 (18.5)	18 (27.3)	259 (18.9)	0.105
Medium	1064 (81.5)	48 (72.7)	1112 (81.1)	
Mismatch ratio*	5.7 (2.6–31.0)	6.3 (3.8–10.2)	5.7 (2.6–30.4)	0.972
Mismatch volume*	46.5 (30.0–78.0)	47.0 (21.0–77.5)	46.9 (29.9–78.0)	0.596
Core volume (ml)*	5.0 (0.1–19.1)	12.0 (1.0–17.0)	5.0 (0.1–19.0)	0.354
Time to imaging*	2.5 (1.5–4.4)	2.9 (2.0–4.9)	2.5 (1.5–4.5)	0.197
Hypoperfusion intensity ratio (HIR)*	0.2 (0.1–0.3)	0.2 (0.1–0.2)	0.2 (0.1–0.3)	0.669

\*Median (IQR).

MT: mechanical thrombectomy; IVtPA: intravenous tissue plasminogen activator; IQR: interquartile range; NIHSS: The National Institutes of Health Stroke Scale; mRS: modified Rankin score; ASPECT: The Alberta Stroke Program Early CT Score.

1135/1307, 88.3%;  $p < 0.001$ , respectively). Patients with perforation were less likely to have an excellent outcome (mRS 0–1 at 3 months) than those without perforation (15/66, 22.7% vs 478/1307, 36.6%;  $p = 0.031$ ).

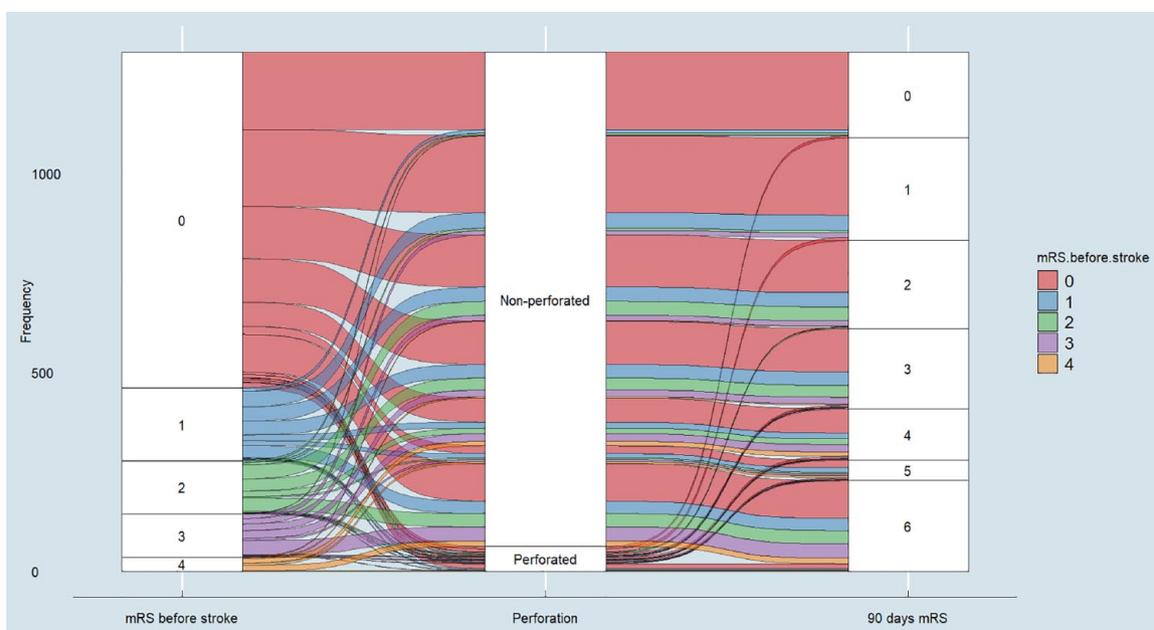
Similarly, the rate of good functional outcomes (mRS 0–2 at 3 months) was also significantly lower in the perforation group compared to non-perforation group (19/66, 28.8% vs 704/1307, 53.9%;  $p < 0.001$ ) (Figures 1 and 2).

**Table 2.** Periprocedural details of the included patients in the study.

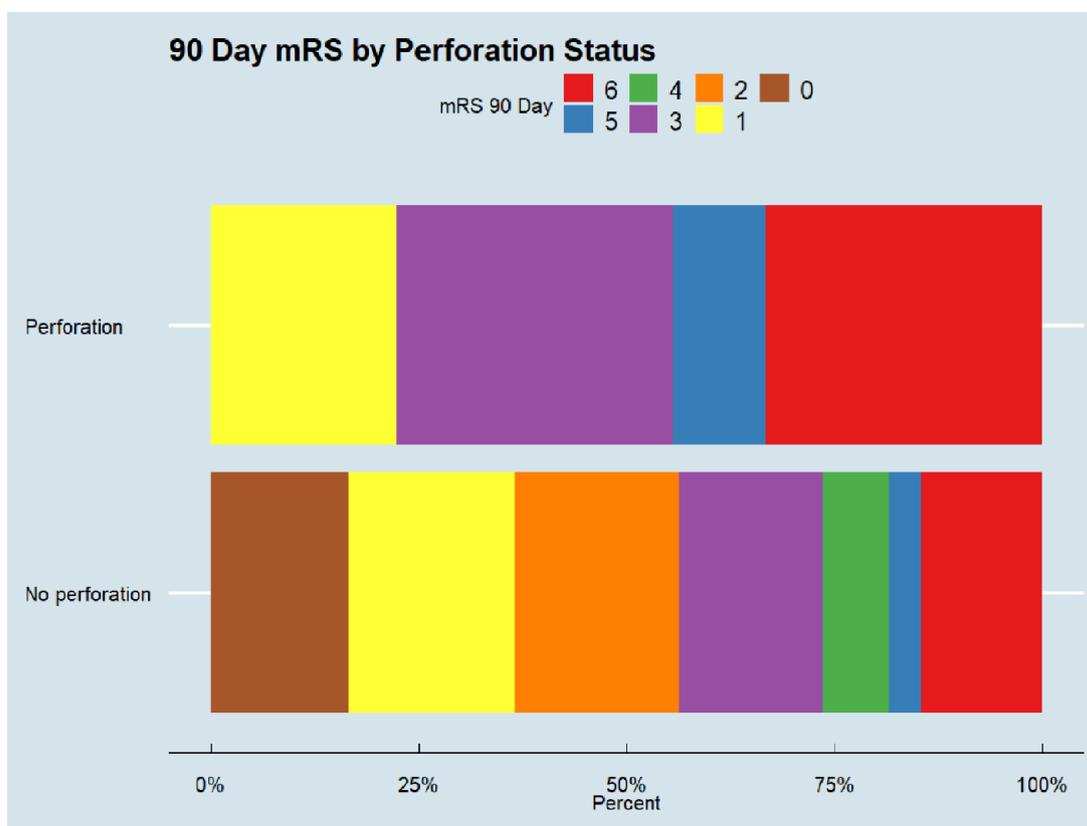
Variable	No perforation	Perforation	Total	p Value
First line technique				
Aspiration	278 (21.3)	8 (12.3)	286 (20.9)	0.083
Stent retriever	198 (15.2)	7 (10.8)	205 (15.0)	
Both	827 (63.5)	50 (76.9)	877 (64.1)	
Given IV tPA	617 (47.2)	36 (54.5)	653 (47.6)	0.299
Mothership versus drip and ship				
Drip and ship	533 (42.9)	28 (44.4)	561 (43.0)	0.913
Mothership	709 (57.1)	35 (55.6)	744 (57.0)	
Onset to arterial puncture (min)*	260.0 (172.0–408.5)	274.5 (201.8–367.8)	260.0 (175.0–407.5)	0.33
Arterial puncture to recanalization time (min)*	0.6 (0.4–0.9)	0.7 (0.5–1.0)	0.6 (0.4–0.9)	0.121
Onset to recanalization (min)*	311.0 (223.0–471.8)	340.0 (264.0–451.0)	314.0 (225.0–471.5)	0.161
Pre-operative SBP*	150.0 (131.8–167.0)	157.5 (143.5–180.0)	150.0 (132.0–168.0)	0.012
Pre-operative DBP*	83.0 (74.0–95.0)	90.0 (80.0–100.0)	83.0 (74.0–95.8)	0.013
Pre-operative temperature (Celsius)*	36.5 (36.1–36.8)	36.5 (36.0–36.9)	36.5 (36.1–36.8)	0.886
Pre-operative glycemia (mg/dl)*	121.0 (103.6–147.0)	115.2 (101.6–145.9)	121.0 (103.6–147.0)	0.622
Pre-operative HR*	79.0 (69.0–94.0)	80.0 (67.5–94.0)	79.0 (69.0–94.0)	0.953
Anesthesia				
General anesthesia	408 (31.4)	25 (37.9)	433 (31.7)	0.361
Local anesthesia	165 (12.7)	10 (15.2)	175 (12.8)	
Sedation	727 (55.9)	31 (47.0)	758 (55.5)	
Puncture site				
Femoral	836 (95.9)	38 (95.0)	874 (95.8)	0.899
Carotid	2 (0.2)	0 (0.0)	2 (0.2)	
Radial	34 (3.9)	2 (5.0)	36 (3.9)	
Periprocedural heparin	99 (9.3)	9 (17.0)	108 (9.7)	0.11
Imaging after MT				
CT	853 (68.3)	50 (78.1)	903 (68.8)	0.154
CT and MR	177 (14.2)	4 (6.2)	181 (13.8)	
MR	218 (17.5)	10 (15.6)	228 (17.4)	
None	0 (0.0)	0 (0.0)	0 (0.0)	

\*Median (IQR).

MT: mechanical thrombectomy; IVtPA: intravenous tissue plasminogen activator; IQR: interquartile range; NIHSS: The National Institutes of Health Stroke Scale; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate.



**Figure 1.** Sankey diagram depicts the transition of mRS scores before stroke versus 90 days after, grouped by perforation status. Colored streams represent the flow of patients from initial mRS scores (0–4) to 90-day outcomes (0–6).



**Figure 2.** Bar charts display the percentage distribution of 90-day modified Rankin Scale (mRS) scores for stroke patients.

In addition, the perforation group had a higher mortality rate than the non-perforation group (20/66, 30.3% vs 220/1307, 16.8%;  $p=0.008$ ). Hemorrhagic complications, including different types of intracranial hemorrhage (ICH), were notably higher in the perforation group ( $p < 0.001$ ) (Table 3).

## Discussion

In this multicenter, retrospective study, we observed an overall low 4.8% incidence of vessel perforation among AIS patients with MeVO undergoing MT. Vessel perforation was associated with poor functional outcomes, increased mortality rates, and higher hemorrhagic complications associated with perforation during MT.

Our results aligns with previous studies as they reported a frequency of perforation during thrombectomy of between 0.7% and 6.9%.<sup>7,8–22</sup> Moreover, our study substantiates the hypothesis generated by Schulze-Zachau et al.<sup>23</sup> that a higher frequency of perforations might characterize MeVO thrombectomy.

Clinical evidence for EVT in DMVOs is still somewhat limited but growing. Randomized trials have largely focused on occlusions in the M2 segment of the middle cerebral artery (MCA), particularly those more proximal and larger, resembling M1 MCA occlusions.<sup>24</sup> Nevertheless,

pooled data from multiple studies, such as the HERMES collaboration, indicated that EVT can benefit certain DMVOs, showing promising results in reperfusion and functional outcomes.<sup>25</sup>

For DMVOs other than M2 MCA, most of the evidence stems from case series. For example, one single-center series showed that EVT achieved high reperfusion rates and had a low complication profile in patients with various types of DMVOs.<sup>26</sup>

Several meta-analyses using nonrandomized data have recently assessed EVT's benefit in MeVOs, suggesting promising safety and efficacy.<sup>27–33</sup> However, the risk of perforation during mechanical thrombectomy remains a serious complication, often linked to poor functional outcomes or even mortality.<sup>23</sup>

Schulze-Zachau et al.<sup>23</sup> discussed that functional outcomes were generally poor for patients experiencing perforation during MT. They reported that 15.8% of patients had an mRS score of 0–1 at 3 months and 25.7% had an mRS score of 0–2 at 3 months. Moreover, the mortality rate in their study was 50.5%. In the present study, 22.7% and 28.8% of patients had mRS scores of 0–1, 0–2, respectively. In addition, the mortality rate in the perforation group was 30.3%. Our findings in addition to Schulze-Zachau et al.<sup>23</sup> highlight the poor outcomes associated with perforation in MeVOs.

**Table 3.** Treatment outcomes of the included patients in the study.

Variable	No perforation	Perforation	Total	p Value
TICI 2c-3	757 (58.9)	14 (23.0)	771 (57.3)	<0.001
TICI 2b-3	1135 (88.3)	35 (56.5)	1170 (86.9)	<0.001
FPE	439 (35.9)	1 (1.7)	440 (34.3)	<0.001
90-day mRS 0–1	478 (36.6)	15 (22.7)	493 (35.9)	0.031
90-day mRS 0–2	704 (53.9)	19 (28.8)	723 (52.7)	<0.001
90-day mortality	220 (16.8)	20 (30.3)	240 (17.5)	0.008
Intracranial hemorrhage (any type)	380 (34.2)	51 (82.3)	431 (36.8)	<0.001
Intracranial hemorrhage (by type)				
HI1	192 (17.3)	23 (37.1)	215 (18.3)	<0.001
HI2	32 (2.9)	1 (1.6)	33 (2.8)	
PH1	29 (2.6)	5 (8.1)	34 (2.9)	
PH2	28 (2.5)	2 (3.2)	30 (2.6)	
SAH	99 (8.9)	20 (32.3)	119 (10.2)	

FPE: first pass effect; TICI: thrombolysis in cerebral infarction; mRS: modified Rankin Score; HI: hemorrhagic infarction; PH: parenchymatous hematoma; SAH: subarachnoid hemorrhage.

Our study has several limitations. First, the retrospective design inherently carries the risk of selection bias. Second, the study did not capture long-term outcomes beyond the 90-day follow-up, limiting our understanding of the lasting impact of perforations during MT on functional recovery and quality of life. Finally, while providing valuable insights into predictors of perforation, our multivariable logistic regression model may not have accounted for all potential confounding variables, such as operator experience or variations in institutional protocols.

## Conclusion

In conclusion, this multicenter, retrospective study provides valuable insights into the incidence and clinical outcomes of perforations during MT in patients with AIS caused by medium vessel occlusion. Our findings indicate that while perforations are relatively rare, they are associated with poorer functional outcomes, higher mortality rates, and hemorrhagic complications. These results underscore the need for heightened awareness and possibly specialized training for managing the risks associated with MT in this specific patient population. Further prospective studies and randomized trials are warranted to substantiate these findings and develop risk mitigation strategies.

## Declaration of conflicting interest

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## Informed consent and ethical approval

The study received approval from the local ethical standards committee at each participating site, and informed consent from patients was waived. The data supporting this study's findings are available from the corresponding author upon reasonable request.

**Guarantor**

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