

EVT 2.0

Distal Vessels and Lytics After Thrombectomy

Four randomized trials, one guideline, and one number that separates them

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Where we're going

1 The territory

A quarter of strokes have a visible occlusion — and we still can't agree what an M2 is

2 Four trials, not three

DISTAL, ESCAPE-MeVO and DISCOUNT were neutral. ORIENTAL-MeVO was not.

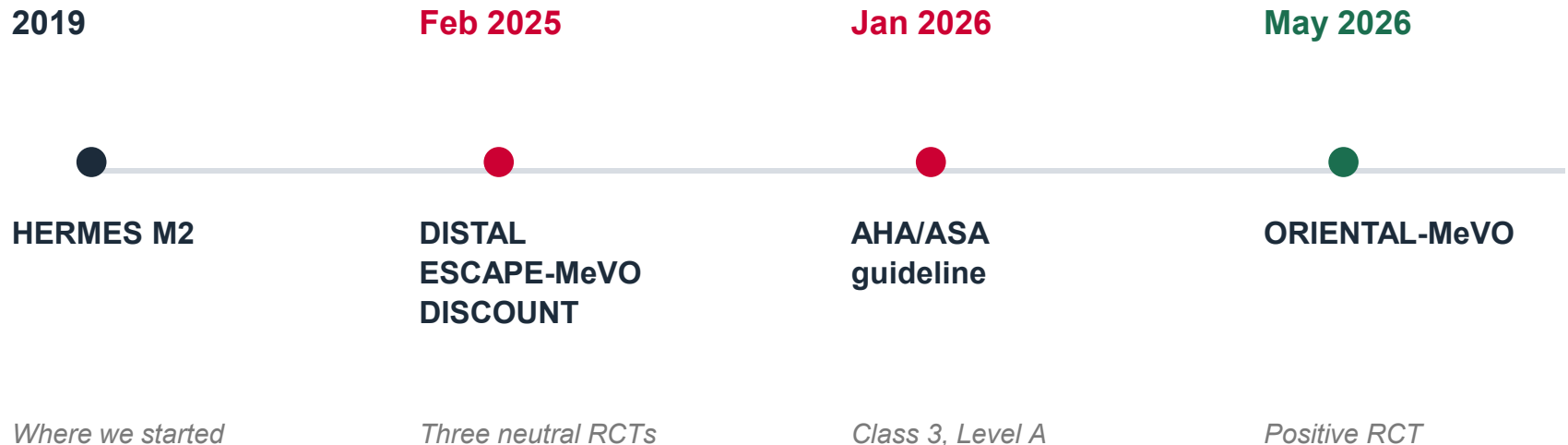
3 The guideline

AHA/ASA 2026 — and the SVIN society statement — both closed before the fourth trial

4 The salvage

Intra-arterial lytics: positive in aggregate, and least convincing exactly where we need it

Eighteen months that inverted twice



The guideline is already one trial out of date. Its Class 3, Level A language was written four months before a 563-patient randomized trial reported a benefit in a population it did not cover.

Prabhakaran S, et al. *Stroke*. 2026;57:e00-e00. doi:10.1161/STR.0000000000000513 (published online January 26, 2026). · Hu W, et al. *N Engl J Med*. 2026;394:1894-1904. doi:10.1056/NEJMoa2514120 (May 14/21, 2026).

01

The territory

Check the denominator — and the definition

MeVO: how common is it, really?

29%

of ischemic strokes have ANY
visible arterial occlusion

1–3 mm

vessel diameter

1 in 2

do not reach mRS 0–1 at 90 days
on best medical management

Check the denominator

Dijon population registry, 971 imaged strokes:
284 (29.2%) any visible occlusion — 167 (17.2%)
proximal anterior, leaving ~117 non-proximal.

“25–40%” is a share of OCCLUSIONS,
not of all ischemic strokes.

Which vessels, and why unanswered

M2–M4 (MCA) · A2–A3 (ACA) · P2–P3 (PCA)

Excluded outright from ESCAPE, SWIFT PRIME,
REVASCAT, THRACE, PISTE; undersampled in
MR CLEAN and EXTEND-IA.

And intravenous thrombolysis does not reliably open them: recanalization on follow-up CTA in only 47.2% of alteplase-treated MeVO (21.4% without).

Denominator: Duloquin G, et al. Stroke. 2020;51:2122-2130 (Dijon Stroke Registry, population-based). PMID 32486967. · Natural history: Ospel JM, et al. Stroke. 2020;51:3232-3240 (n=258, median NIHSS 7).

We still don't agree on what an M2 is

Four trials. Four definitions. None of them the guideline's.

	How each source defined the M2 it was talking about
AHA/ASA 2026 guideline	Dominant = “the M2 segment supplying 50% or more of the MCA territory”
DISTAL	Nondominant or codominant M2, plus M3 and M4 — dominant M2 excluded
ESCAPE-MeVO	Proximal M2 = bifurcation to 1 cm distal; distal M2 to the circular sulcus; M3 = opercular. Proximal M2 enrolled (25%) — dominance never recorded
DISCOUNT	Only M2 distal to the mid-height of the insula — proximal M2 excluded by design
ORIENTAL-MeVO	Codominant or nondominant M2 with vessel diameter ≤ 2.0 mm — dominant M2 excluded

So no trial has ever tested the subgroup the guideline preserved. Three of the four excluded dominant or proximal M2 outright;
the fourth enrolled proximal M2 but never adjudicated dominance.

DISTAL: N Engl J Med. 2025;392:1374-1384. · ESCAPE-MeVO: N Engl J Med. 2025;392:1385-1395 (segment definitions, Table S1 footnote). · DISCOUNT: JAMA. 2026. · ORIENTAL-MeVO: N Engl J Med. 2026;394:1894-1904. · Dominance definition: 2026 AHA/ASA guideline.

The case for M2 before 2025

Pooled patient-level data, 7 randomized trials · n = 130 M2 occlusions (116 proximal, 73 dominant) · successful reperfusion 59.2%

Subgroup	n	Outcome	Adjusted OR (95% CI)
All M2	130	90-d mRS 0–2: 58.2% vs 39.7%	2.39 (1.08–5.28), p=0.03
Proximal M2	116	90-d mRS 0–2	2.68 (1.13–6.37)
Dominant M2	73	90-d mRS 0–2	4.08 (1.08–15.48)
sICH	130	0 of 67 with EVT vs 5 of 63 control	see note — tiny numbers

Say the quiet part: n = 130 drawn from seven trials, in patients who met LVO-trial protocols. The dominant-M2 interval spans a factor of fourteen, and the hemorrhage numbers are 5 events.

Never the same grade of evidence as the M1 data — and note these patients had LVO-trial severity. It was not the only pooled M2 dataset.

We knew this in 2022

“Functional independence was more frequent with EVT in patients with moderate or severe strokes, as defined by baseline NIHSS above any thresholds from 6 to 10, whereas there was no difference between groups with milder strokes below these thresholds.”

Sarraj et al., Annals of Neurology, 2022 · pooled patient-level analysis of 517 isolated M2 occlusions

Sarraj 2022 · n = 517

mRS 0–2 68.3% vs 61.6% aOR 2.42 (1.25–4.67)

Mortality 5% vs 10% aOR 0.32 (0.12–0.87)

Benefit only with perfusion mismatch

Guo 2023 · n = 4,358

NIHSS ≥ 6: mRS 0–2 OR 1.82 (1.34–2.49)

NIHSS 0–5: mRS 0–2 OR 0.81 (0.59–1.10)

NIHSS 0–5: sICH OR 4.21 (1.86–9.49)

LEVEL OF EVIDENCE: neither is randomized evidence for MeVO. Sarraj pools 3 RCTs with 2 prospective non-randomized cohorts; Guo pools 20 mostly observational studies.

02 The randomized evidence

Three trials said no. One said yes. The difference was the patient.

The four randomized trials

	DISTAL	ESCAPE-MeVO	DISCOUNT	ORIENTAL-MeVO
n	543	530	244	563
Country	11 countries	5 countries	France	China
Window	≤ 24 h	≤ 12 h	≤ 8 h (24 h FLAIR-)	≤ 24 h
Entry NIHSS	≥4 or disabling	>5, or 3–5 disabling	—	≥ 6
Median NIHSS	6	8	8	10
Median age	77	—	75	71
IVT	65.4%	58%	—	36.6%
Primary outcome	90-d mRS shift	90-d mRS 0–1	90-d mRS 0–2	90-d mRS 0–2
Rates	—	41.6% vs 43.1%	62% vs 68%	58.6% vs 46.6%
Effect	cOR 0.90 (0.67–1.22)	aRR 0.95 (0.79–1.15)	OR 0.73 (0.40–1.31)	aRR 1.24 (1.07–1.44)
sICH	5.9% vs 2.6%	5.4% vs 2.2%	11% vs 3%*	4.7% vs 2.2%
90-d mortality	15.5% vs 14.0%	13.3% vs 8.4%	6% vs 8%	11.1% vs 10.2%
12-month	acOR 0.81 (0.59–1.12)	not reported	not reported	not reported

*DISCOUNT sICH is as-treated, not by randomized arm. · DISTAL: *N Engl J Med.* 2025;392:1374-1384 and *Lancet Neurol.* 2026;25:571-580. · ESCAPE-MeVO: *N Engl J Med.* 2025;392:1385-1395. · DISCOUNT: *JAMA.* 2026. · ORIENTAL-MeVO: *N Engl J Med.* 2026;394:1894-1904.

The three neutral trials, side by side

	DISTAL	ESCAPE-MeVO	DISCOUNT
Size and sites	543 · 55 sites, 11 countries	530 · 5 countries	244 · 22 French centers
Occlusions	M2 44% · M3 27% · P2 13%	84.7% MCA branch	M3 76%
mRS result	shift cOR 0.90 (0.67–1.22)	0–1: 41.6% vs 43.1% aRR 0.95 (0.79–1.15)	0–2: 62% vs 68% OR 0.73 (0.40–1.31)
sICH	5.9% vs 2.6%	5.4% vs 2.2%	11% vs 3% (as-treated)
90-d mortality	15.5% vs 14.0%	aHR 1.82 (1.06–3.12)	6% vs 8%
What ended it	completed; 12-month acOR 0.81	completed	stopped early at interim: futility + excess sICH

Put that hemorrhage row next to 2015. In the pooled LVO trials (HERMES, n = 1,287) symptomatic hemorrhage did **not differ** between thrombectomy and control.

In MeVO it roughly doubles to triples — in every trial. Same operators, same devices, smaller vessel.

DISTAL: N Engl J Med. 2025;392:1374-1384 and Lancet Neurol. 2026;25:571-580. · ESCAPE-MeVO: N Engl J Med. 2025;392:1385-1395. · DISCOUNT: JAMA. 2026. · LVO comparison: Goyal M, et al. Lancet. 2016;387:1723-1731 (HERMES).

ORIENTAL-MeVO

The trial the guideline never saw · open-label RCT, blinded outcome · 48 centers, China · n = 563 · NIHSS ≥ 6

58.6% vs 46.6%

90-day mRS 0–2
aRR 1.24 (1.07–1.44), P = 0.004

NNT 8

one extra independent patient
per 8 treated (12.0% absolute)

NIHSS 10

median presenting severity
(vs 6, 8 and 8 in the neutral trials)

	Thrombectomy (n=280)	Control (n=283)
sICH	4.7%	2.2%
90-day mortality	11.1%	10.2%
IV thrombolysis	36.6%	36.6%

For scale: in the 2015 LVO trials the published NNT was 2.6 to improve disability by at least one mRS level (HERMES, n = 1,287, adjusted cOR 2.49).

Different endpoint, so not a like-for-like number — but the direction is unmistakable. MeVO's effect is real and several times smaller.

What a one-point shift actually means

Every odds ratio in this talk is about moving someone across one of these lines.



mRS 1–2

Back home. Back to work or most of it.

May not manage everything they used to — but needs nobody.



mRS 3

Walks, but needs help.

Cannot be left for a full day. Someone reorganizes their life around this.



mRS 4

Cannot walk or toilet without assistance.

Full-time carer, or a facility. Usually the end of independent living.

above this line = functionally independent



mRS 5

Bedbound, incontinent, constant nursing.

Many patients and families say they would not have wanted this.

Descriptions are the conventional clinical reading of the modified Rankin Scale, written in plain language for a lay audience; they are not quoted from a scale manual.

DISTALS: a device built for the vessel

Tigertriever 13, radially adjustable low-profile stent retriever · US/Europe FDA-IDE, randomized, blinded endpoint · 118 randomized, IVT-ineligible

NIHSS 7.3

baseline severity (± 4.5)
same mild population as the neutral trials

86.3% vs 27.7%

PRIMARY: reperfusion at 24 h
without sICH ($P < 0.001$)

41.2% vs 38.2%

90-day mRS 0–1
no CI or P value published

	DISTALS
Population	IV-thrombolysis–INELIGIBLE, within 24 h. Non-/co-dominant M2 41% · M3 25% · PCA 25% · ACA 9%. Last-known-well to randomization 511 min
90-day clinical	mRS 0–1 41.2% vs 38.2%. Among those mRS 2–5 at baseline, 69% vs 56% improved by ≥ 1 level. Similar 90-day survival
Safety	sICH 1.6% vs 0% (ITT); zero sICH in patients actually treated with the device, including all 28 with M3 occlusion

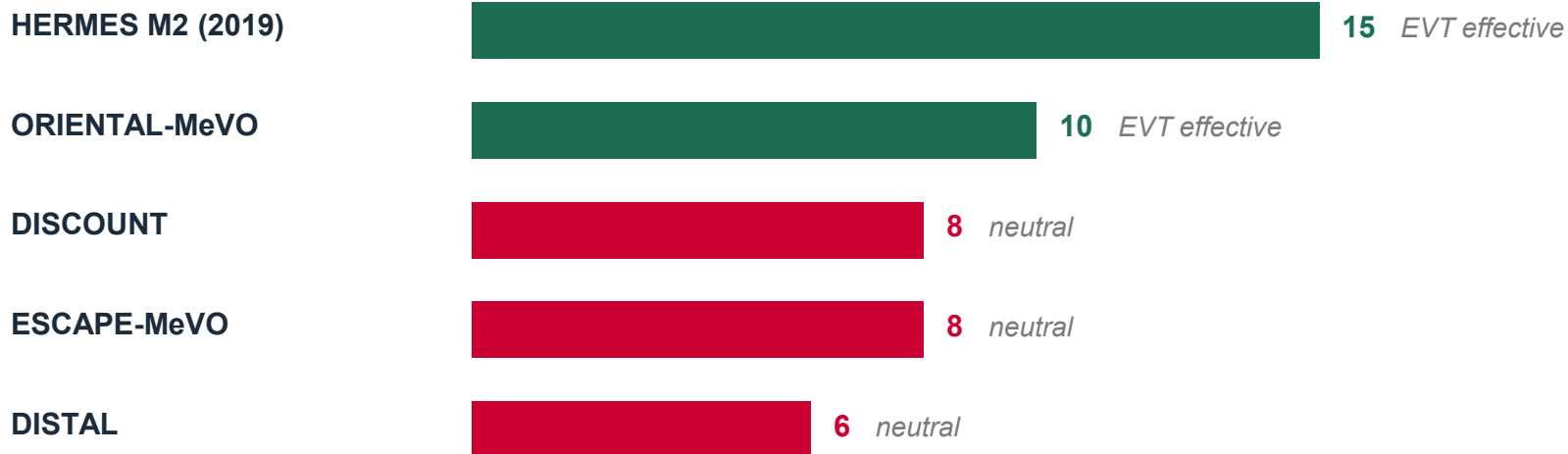
The device worked. The patients did not clearly do better. A 3-point difference in mRS 0–1, reported without a confidence interval or P value.

Same NIHSS 7 population as the trials that failed — a better tool aimed at the same mild stroke.

Primary endpoint and baseline: Saver J, et al. *Eur Stroke J.* 2026;11(Suppl 1):i992-i993. · 90-day outcomes presented at ESOC 2026 (Maastricht, 6–8 May); from conference reporting and sponsor release — not peer-reviewed.

What separates them

Median presenting NIHSS across every dataset in this talk — the guideline makes this comparison itself



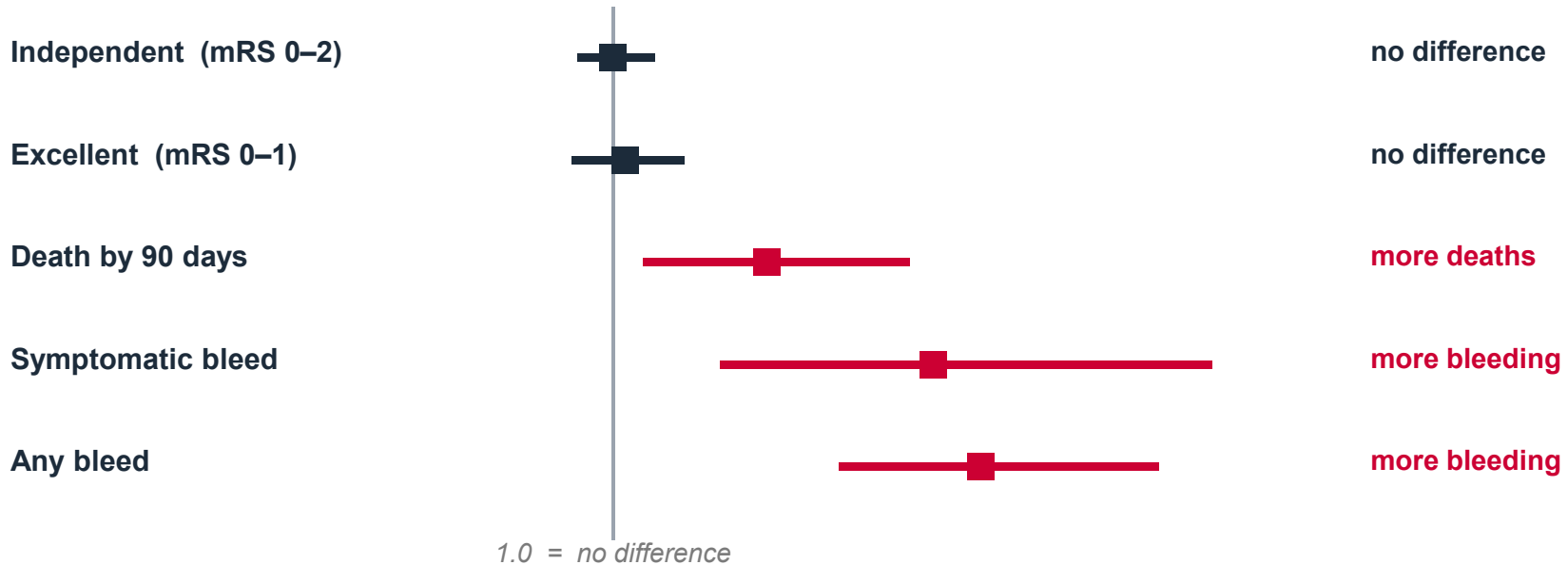
Tested formally, in the most distal territory of all. Registry of 1,075 M3/M4, ACA and PCA occlusions:
NIHSS ≥ 6 — aRR 1.61 (1.37–1.92) favoring EVT. NIHSS 1–5 — aRR 0.79 (0.58–1.19). P for interaction < 0.001 .

Same threshold Sarraj 2022 and Guo 2023 had already identified, three years before the trials reported.

NIHSS: Menon 2019 (HERMES M2); DISTAL median 6 (IQR 5–9); ESCAPE-MeVO median 8 (IQR 5–11); DISCOUNT median 8 (IQR 6–12); ORIENTAL-MeVO median 10. · Registry: Jing X, Chen Z, Zhao Y, et al. Radiology. 2025;317(2):e251040. PMID 41288486.

Pooled: no gain, more bleeding

38 studies · 4,584 treated vs 5,468 medically managed · every estimate below predates ORIENTAL-MeVO



And the reperfusion rate was 78% — which is not the reassurance it sounds like.

78% is mTICI 2b or better. It says nothing about how many passes it took, how long it took, or how many reached 2c–3 — and in a small territory those are the things that decide whether reperfusion is worth anything.

Palaodimou L, Safouris A, Papageorgiou NM, et al. Neurology. 2025;105:e214015. · RCT-only estimates agree: Zhou HJ, et al. J Am Heart Assoc. 2025;14:e042299 (3 RCTs, n=1,246).

Why were the first three neutral?

Severity

median NIHSS 6–8 vs 15 in HERMES M2 and 10 in ORIENTAL-MeVO

Pooled territories

MCA branches pooled with ACA and PCA — isolated PCA EVT alone carries mortality OR 1.81 (1.24–2.65)

Prestroke disability

allowed in DISTAL and ESCAPE-MeVO

Technique

stent-retriever first-line; aspiration predicted first-pass effect in M2 (75% vs SR, $p=0.007$)

Reperfusion

~78% vs 80–90% in the LVO trials

Background IVT

58–65% — dilutes the treatment contrast

Device–vessel mismatch

device >20% larger than the vessel: sICH OR 3.32 (1.04–10.64)

Endpoint

mRS 0–1 / 0–2 for often single-domain cortical syndromes

None of these is a reason to ignore the trials. Each is a reason the fourth one differed.

What was actually done in the trials

	DISTAL	ESCAPE-MeVO	DISCOUNT	ORIENTAL-MeVO
First-line technique	combined 67% aspiration 16% · SR 17%	Solitaire X mandated first-line by protocol	SR for distal vessels, or aspiration	combined 46.9% aspiration 20.2% · SR 9.5%
Passes, median	1 (IQR 1–2)	not reported	1.5 (IQR 1–2)	not reported
General anesthesia	47–54%	43.1%	all three permitted	33.9%
Successful reperfusion	82.4% comb · 76.5% aspir 61.1% SR only	75.1% (MeVO-eTICI 2b–3)	85% mTICI ≥2b 68% eTICI 2c–3	74.4%
Onset to reperfusion	294 min to start	359 min to recanalization	258 min to start	6.4 h to revascularization
IA lytic used	3 of 222 patients	—	—	53 of 262 (20.2%)

ESCAPE-MeVO's own comparison: 359 minutes from onset to recanalization, against 241 minutes in ESCAPE — their own LVO trial.

We took two hours longer to open a smaller vessel with less collateral reserve.

DISTAL technique subanalysis: Schulze-Zachau V, et al. J Neurointerv Surg. 2025. doi:10.1136/jnis-2025-024374. · ESCAPE-MeVO: N Engl J Med. 2025;392:1385-1395. · DISCOUNT: JAMA. 2026 (cross-trial onset-to-start times are DISCOUNT's own compilation). · ORIENTAL-MeVO: N Engl J Med. 2026;394:1894-1904.

The DISTAL technique subanalysis

222 patients, 35 different clot retrievers and 18 aspiration catheters, adjudicated by the trial core lab

	Combined (n=149)	Aspiration (n=36)	Stent retriever (n=37)
First-pass reperfusion	66.4%	44.4%	59.5% (P = 0.049)
Final mTICI ≥2b	82.4%	76.5%	61.1% (P = 0.021)
Final mTICI ≥2c	61.5%	61.8%	52.8% (P = 0.62)
Passes, median	1 (1–2)	2 (1–2.2)	2 (1–3)
Puncture→reperfusion	36 min	30 min	36 min
Balloon guide catheter	36.2%	25.0%	70.3% (P < 0.001)
Switched technique after pass 1	18.6%	61.9%	25.0% (P < 0.001)
Any ICH / SAH	45.6% / 30.9%	27.8% / 19.4%	40.5% / 29.7%
sICH	7.4%	2.8%	8.1%
90-day mRS 0–2	53.7%	58.3%	54.0%

No technique won on outcome. Combined opened more vessels; aspiration bled less and switched more; stent retriever alone opened fewest.

Vessel perforation: 1 in 76 aspiration passes, 6 in 271 combined, none after a stent-retriever pass.

Schulze-Zachau V, Rommers N, Dobrocky T, et al. J Neurointerv Surg. 2025. doi:10.1136/jnis-2025-024374. PMID 41339078. · Technique was operator-chosen, so these comparisons are observational within a randomized trial.

The margin is thinner, so technique costs more

In LVO the absolute benefit absorbs a complication. In a 2 mm vessel it does not.

Stent retriever

Must cross the clot with microwire and microcatheter — in a tortuous distal branch that is where perforation and subarachnoid blood come from.

Device >20% wider than the vessel:
sICH OR 3.32 (1.04–10.64)

Aspiration

Engages the proximal face without traversing the clot.

In M2, independently predicted first-pass effect over stent retriever ($p = 0.007$), and first-pass effect predicted 90-day independence: 83.3% vs 60.3%

Vessel perforation in distal thrombectomy, 1,373 patients: **4.8% overall**

M3 8.9% A2 8.3% proximal M2 4.3% — predictors: smaller vessel, more distal, tortuosity, longer procedure.

SVIN 2026, verbatim: “in DMVO, where the efficacy gap between best medical management and EVT is narrower, even a modest increase in procedure-related complications may negatively influence the clinical outcome and offset the treatment effect.”

Perforation: multicenter DMVO series, $n=1,373$, reported in the SVIN 2026 statement. · Device–vessel ratio: Virtanen P, et al. Eur Stroke J. 2025 ($n=146$). · Aspiration and first-pass effect: Navia P, et al. J Neuroimaging. 2025 ($n=108$). · Technique comparison: DISTAL subanalysis, J Neurointerv Surg. 2025.

Tissue saved. Patients not.

DISTAL post hoc · JAMA Neurol 2026

n = 447 · imaging at median 22.9 h

≥80% of tissue-at-risk spared:

aOR 1.6 (95% CI 1.1–2.3) with EVT

aOR 2.5 (1.3–4.8) with successful
reperfusion

Better imaging outcome → better 90-day
clinical outcome in both arms.

ESCAPE-MeVO post hoc · JNIS 2026

253 of 255 EVT patients scored;
only 52.2% reached meTICI 2c–3

meTICI 2c–3 vs usual care:

lower infarct volumes, but

90-day mRS adjusted cOR 1.17
(95% CI 0.79–1.75)

Higher meTICI → better mRS within EVT.

Two trials, two imaging analyses, one answer: the intervention does what we believe it does to tissue, and in a mildly affected population that is not enough to move a 90-day disability scale.

03

The guideline

AHA/ASA 2026 — written before the fourth trial reported

2026 AHA/ASA — what it actually says

	Recommendation	COR	LOE
EVT #7	Dominant proximal M2 MCA, <6 h, prestroke mRS 0–1, NIHSS ≥6, ASPECTS ≥6 — “EVT is reasonable... but the benefits are uncertain”	2a	B-NR
EVT #8	Proximal nondominant or codominant M2, distal MCA, ACA, or PCA — “EVT is not recommended to improve functional outcomes”	3: No Benefit	A
Tech #5	Medium or distal vessels (nondominant/codominant M2, M3, PCA) — “EVT with stent retrievers is of no benefit”	3: No Benefit	A
Tech #8	After mTICI ≥2b — adjunctive intra-arterial urokinase, alteplase or tenecteplase “may be reasonable”	2b	B-R

Guideline's own definition: “Dominant is defined as the M2 segment supplying 50% or more of the MCA territory.”

The guideline's own reading of the trials

From the recommendation-specific supportive text — the part nobody reads

Verbatim, on ESCAPE-MeVO:

“The study generally recruited patients with less severe symptoms at presentation, with a median NIHSS score of 8, compared with the median NIHSS score of 15 in the patients included in the previous meta-analysis who had shown benefit.”

What else it concedes

Proximal M2 subgroup (n = 122):
risk ratio 0.9 (95% CI 0.6–1.33)

“ESCAPE-MeVO did not include considerations
for dominance versus codominance”

Workflow times longer than in LVO trials

And how it defines proximal M2

“MCA segment proximal to the point that
was 1 cm distal to the MCA bifurcation”

— ESCAPE-MeVO’s definition, adopted verbatim
into the guideline’s supportive text.

The guideline made the severity argument itself. Then it wrote Class 3, Level A — because in January 2026 there was no trial that had tested the more severe population.

Prabhakaran S, et al. Stroke. 2026;57:e00-e00. doi:10.1161/STR.0000000000000513, endovascular thrombectomy recommendation-specific supportive text. ·
ESCAPE-MeVO median NIHSS 8 (IQR 5–11) per N Engl J Med. 2025;392:1385-1395.

The guideline told us what to do next

“Knowledge Gaps and Future Research”, quoted in full

“The efficacy of EVT in medium vessel occlusions treated with faster workflows, using different techniques (aspiration-first, IA thrombolysis, or new devices) in patients with more substantial neurological deficits at presentation requires further investigation.”

“The development and evaluation of new EVT techniques designed for medium and distal vessels also require further research.”

“The role of EVT in patients with moderate prestroke morbidity and those with low NIHSS scores at presentation requires investigation in future RCTs.”

Read that first bullet again. The guideline named intra-arterial thrombolysis and more substantial deficits as its two open questions. Four months later ORIENTAL-MeVO answered the second one.

And the society statement: SVIN 2026

A focused SVIN statement, not a guideline in the AHA/ASA sense — but it goes territory by territory, which the guideline does not.

Territory	Recommendation	COR	LOE
M2	EVT should be performed for disabling proximal and/or dominant M2 occlusions, with favorable imaging	Ia	B-NR
M2	EVT is reasonable in nondominant/codominant or distal M2 with severe presentation (NIHSS ≥ 6)	IIb	B-R
M2	Routine EVT for nondominant or low-severity M2 is not recommended	III	A
M3 / M4	Routine EVT not recommended; may be considered in select cases with severe deficits and favorable imaging	III / IIb	B-R / C-LD
ACA (A2/A3)	Routine EVT not recommended; consider if disabling deficit and large territory at risk	III / IIb	B-NR
PCA (P1–P3)	Routine EVT not recommended; may be considered for severe disabling deficits or if IVT not possible	III / IIb	B-NR / B-R

Verbatim conclusion: *“Routine EVT for DMVO is not supported by current evidence; however, performing EVT in patients with disabling acute dominant M2 occlusion remains reasonable.”*

Majidi S, Mehta A, Al-Kasab S, et al. *Stroke Vasc Interv Neurol.* 2026;6:e002314. · Graded by SVIN GAPS criteria (III = no benefit; B-R = single RCT or RCT subgroup; B-NR = observational; C-LD = limited data).

Using a guideline that is already behind

What still holds

Dominant proximal M2, disabling deficit — guideline 2a; the SVIN statement calls it “reasonable.”

Class 3 / Level A is correct for the population the first three trials enrolled.

Stent retrievers in 1–3 mm vessels — the device-specific warning still stands.

What has moved since

ORIENTAL-MeVO: 563 patients, NIHSS ≥ 6 , positive primary outcome — published after both documents closed.

Aspiration and combined approach: unaddressed by the guideline or the SVIN statement, not disproven.

IA thrombolysis: named by the guideline as an open question, now with pooled RCT data behind it.

The guideline’s own words on how to individualize:

“Defining deficits that are disabling for an individual patient is challenged by subjective considerations; a deficit that is disabling for 1 individual may not be for another. Use of the NIHSS score alone does not...”

A guideline is a floor, not a ceiling. The next AIS cycle will not arrive before 2027 — and no one should treat, or withhold, on that timetable.

Quotation from the 2026 AHA/ASA guideline, intravenous thrombolysis recommendation-specific supportive text. · Note also: minor (NIHSS ≤ 3) noncardioembolic AIS without IVT — DAPT 21 days then single antiplatelet is Class 1, Level A. For the mildest MeVO, there is a Class 1 therapy, and it is not thrombectomy.

What the field actually did

Survey of 43 site PIs across 47 US comprehensive stroke centers · 93% response

Occlusion	Treated with MT before the RCTs	Will still treat	Depends on ≥ 1 variable
Nondominant M2	95%	15%	57.5%
All other anterior DMVO	50%	7.5%	32.5%

The most common variable named as decisive: symptom severity.

The field converged on the NIHSS thesis by instinct, a year before a trial tested it.

04 **Lytics after thrombectomy**

Positive in aggregate. Least convincing where we need it.

IA lytic use is off-label/investigational

Full circle

PROACT II · JAMA 1999

9 mg IA pro-urokinase + heparin vs heparin
n = 180 · MCA occlusion < 6 h · 54 centers

90-d mRS ≤2: 40% vs 25% (P = .04)

Recanalization: 66% vs 18% (P < .001)

ICH ≤24 h: 10% vs 2% (P = .06)

Mortality: 25% vs 27%

Where it returned

The first efficacy signal in acute stroke intervention was a drug, delivered intra-arterially, into the MCA.

We abandoned it for hardware. Twenty-seven years later the hardware has hit its limit in exactly the vessels the drug could reach.

The mechanism: macrovascular reperfusion ≠ microvascular reperfusion.

mTICI 2b–3 with persistent no-reflow, distal emboli below angiographic resolution, downstream thrombus in branches a catheter cannot reach. A hypothesis — not a finding.

The intra-arterial lytic randomized trials

Trial	Agent / dose	Population	n	Primary outcome	Result
CHOICE	IA alteplase 0.225 mg/kg	Anterior LVO, eTICI 2b50–3	113	90-d mRS 0–1	59.0% vs 40.4% ARD 18.4% (0.3–36.4)
POST-UK	IA urokinase 100,000 IU	LVO, eTICI 2c–3, no prior IVT	535	90-d mRS 0–1	45.1% vs 40.2% aRR 1.13 (0.94–1.36)
ATTENTION-IA	IA TNK 0.0625 mg/kg	Posterior circulation, eTICI 2b50–3	208	90-d mRS 0–1	34.6% vs 26.0% aRR 1.36 (0.92–2.02)
POST-TNK	IA TNK 0.0625 mg/kg	LVO, eTICI 2c–3, no prior IVT	540	90-d mRS 0–1	49.1% vs 44.1% aRR 1.15 (0.97–1.36)
ANGEL-TNK	IA TNK 0.125 mg/kg	Anterior LVO, 4.5–24 h, eTICI 2b–3	256	90-d mRS 0–1	40.5% vs 26.4% RR 1.44 (1.06–1.95)
IAT-TOP	IA alteplase 0.225 mg/kg	Posterior circulation, successful EVT	246	90-d mRS 0–2	41.9% vs 46.7% aRR 0.93 (0.73–1.18)

Six trials, two positive — and both positives have an asterisk. CHOICE stopped early with 113 of 748 eligible patients randomized; ANGEL-TNK's primary outcome was positive with 0 of 7 secondary endpoints supporting it. **Safety is not uniform either: ATTENTION-IA sICH 8.3% vs 3.1% (aRR 3.09, 0.78–12.20).**

POST-TNK: JAMA. 2025;333:579. · ANGEL-TNK: JAMA. 2025;334:582. · IAT-TOP: JAMA Neurol. 2026 (PMID 42026933). · CHOICE: JAMA. 2022;327:826. · POST-UK: JAMA. 2025;333:589. · ATTENTION-IA: BMJ. 2025;388:e080489.

The dose problem

Two Chinese trials, published the same day, disagree about whether 0.125 mg/kg is safe.

ANGEL-TNK · JAMA 2025

IA tenecteplase 0.125 mg/kg

mRS 0–1: 40.5% vs 26.4%

RR 1.44 (1.06–1.95), $P = .02$

sICH 5.6% vs 6.2%

No safety signal at this dose.

Hou et al. dose-escalation · JAMA Neurol 2025

Phase 1b/2a, $n = 205$

Tiers 0.0313 / 0.0625 / 0.125 / 0.1875

0.125 mg/kg: sICH in 3 of 12 —
exceeded the prespecified safety
threshold ($P = .04$)

Phase 2a: no efficacy signal at either
0.0313 or 0.0625 mg/kg.

Both cannot be the last word. The dose that produced the only positive IA-TNK primary outcome is the dose a parallel dose-finding trial stopped for hemorrhage — and no one has done this work in a 2 mm vessel at all.

Miao Z, Luo G, Song L, et al. JAMA. 2025;334(7):582-591. doi:10.1001/jama.2025.10800. · Hou X, Huang J, Wang L, et al. Intra-arterial tenecteplase after successful reperfusion in large vessel occlusion stroke: a randomized clinical trial. JAMA Neurol. 2025;82(9):895-904. doi:10.1001/jamaneurol.2025.2036.

Pooled, the IA lytic story is positive

Meta-analysis	Included	mRS 0–1	mRS 0–2	sICH
Alkhiri et al. JNIS 2025	7 RCTs 2,131 pts	OR 1.44 (1.21–1.72)	—	OR 1.15 (0.75–1.75)
Guo et al. 2025 (NMA)	7 RCTs 2,128 pts	RR 1.23 (1.11–1.36)	RR 1.04 (0.96–1.13)	RR 1.23 (0.81–1.85)
Gonçalves et al. Neurol Sci 2026	4 RCTs (TNK only) 1,160 pts	RR 1.22 (1.04–1.44), I ² =0%	ns	ns

The asterisk: the benefit lives entirely in mRS 0–1 and disappears at mRS 0–2.

That is a real and defensible effect — moving people from good to excellent — but it is not the effect size that justifies a new step in an already long procedure without knowing who benefits.

All three predate IAT-TOP. Guo's network meta-analysis found no difference between IA alteplase, tenecteplase and urokinase.

ANGEL-TNK by occlusion site

Prespecified secondary analysis · 19 centers · n = 256 · ICA 71 · M1 122 · M2 62

Occlusion site	90-d mRS 0–1	Effect	Any ICH ≤48 h	eTICI progression
ICA	39.4% vs 13.2%	RR 2.99 (1.51–5.96) p = 0.002	15.2% vs 39.5% RR 0.38, p<0.001	51.5%
MCA M1	—	no significant benefit	—	37.9%
MCA M2	—	no significant benefit	—	25.7%

Interaction between ICA and MCA segments significant for both function and safety.

The more distal the occlusion, the less the lytic does. eTICI progression falls monotonically from ICA to M1 to M2 — and the pooled benefit above is carried by the proximal end.

62 M2 patients in a secondary analysis does not close the question either way.

IA lysis for MeVO: what exists

Study	Design	n	Finding
Salim et al. Clin Neuroradiol 2026	MAD-MT registry, 37 centers, PS-matched	184 (19 IAT / 165 MT)	mRS 0–1 38% vs 21% (P=.20); mTICI 2b–3 68% vs 90% (P=.02); sICH 0% vs 6.7%
Cendrero et al. JNIS 2026 (SAIL)	Single-center retrospective series	—	Stent retriever-assisted IA lysis with tirofiban as a pharmacomechanical rescue for M2–M3, A2–A3, P1–P2
Zhu et al. BMC Neurol 2026	oriental-MeVO registry, 25 centers, M3/M4 only	342 (170 EVT / 172 SMM)	mRS 0–1 36.5% vs 37.2%, aRR 0.88 (0.64–1.22); no sICH or mortality difference
ALLY pilot Stroke 2025	Single-center, prospective, non-randomized	20	IA tenecteplase up to 4.5 mg for INCOMPLETE recanalization; any ICH 11/20, sICH 1, 90-d mRS 0–2 50%. Feasibility only
RESCUE-TNK	Phase 2 RCT, rescue IA TNK for MeVO	—	Protocol published; results not yet reported

There is no randomized IA-lytic-for-MeVO evidence. Nineteen matched patients and a single-center technique series is what the entire distal question rests on.

Salim HA, et al. Clin Neuroradiol. 2026. · Cendrero J, et al. J Neurointerv Surg. 2026. · Zhu Y, et al. BMC Neurol. 2026;26:510. · Zaidi SF, et al. Stroke. 2025;56:355-361 (ALLY). · RESCUE-TNK: PMID 37051058.

If not everyone, then who?

MAD-MT registry · 37 centers · 1,007 patients (822 EVT / 185 medical management) · 2017–2023

Clinical need (positive points)

- +1 per NIHSS point
- +7 no intravenous thrombolysis
- predictors of poor outcome on medical management alone

Procedural risk (negative points)

- 1 per 15 years of age above 25
- 2 absence of hypertension
- 2 absence of atrial fibrillation
- predictors of EVT failure or harm

The score modified the effect of EVT versus medical management ($P_{\text{interaction}} = 0.048$)

Score ≥ 15 (n = 293): EVT better — median 90-day mRS 3 vs 4 ($P = 0.009$)

Score < 15 (n = 710): EVT worse — median 90-day mRS 2 vs 1 ($P = 0.014$)

Practice points

- 1** **Dominant proximal M2, disabling deficit — the guideline still says reasonable.**
AHA/ASA 2a, and the SVIN society statement agrees. The Class 3 trials excluded this subgroup.
- 2** **Nondominant/codominant M2, M3, M4, ACA, PCA — Class 3, Level A, and a registry that agrees.**
The burden of proof has flipped. You are the one who has to justify treating.
- 3** **Severity is the discriminator the data keep pointing at.**
NIHSS 6–8 → three neutral trials. NIHSS 10 → ORIENTAL-MeVO positive. NIHSS 15 → HERMES M2. The MAD-MT score reached the same variable from a registry.
- 4** **Technique is unsettled, not settled against us.**
The Class 3 language names stent retrievers. Combined approach gave the best first-pass reperfusion in DISTAL.
- 5** **Adjunctive IA lytic after mTICI $\geq 2b$: real but small, and proximal.**
Pooled benefit is confined to mRS 0–1, and by occlusion site it sits in the ICA — not the MCA branches.

What's coming

Trial	What makes it different	Status
DISTALS	Angiographic primary endpoint (reperfusion without sICH); the only trial enrolling by vessel diameter (≥ 1.5 mm) rather than segment label	Completed NCT05152524
RESCUE-TNK	Phase 2 — rescue intra-arterial tenecteplase specifically for MeVO	Protocol published
PEARL	IA alteplase after mechanical thrombectomy; multicentre, blinded endpoint	Protocol published
IA-SUCCESS	IA thrombolysis after successful recanalization, anterior circulation	Protocol published
INSIST-IT	IA tenecteplase after sufficient recanalization in basilar occlusion	Protocol published
BRETIS-TNK II	IA tenecteplase during thrombectomy	Protocol published

The design question: better-selected patient, better tool, better endpoint — or a drug? ORIENTAL-MeVO just answered for the patient. DISTALS is the only one betting on the endpoint.

DISTALS verified on ClinicalTrials.gov: NCT05152524, completed, no results posted. · RESCUE-TNK PMID 37051058 · PEARL PMID 39500603 · IA-SUCCESS PMID 42439416 · INSIST-IT PMID 37231688 · BRETIS-TNK II PMID 37169399.

Take home

MeVO thrombectomy didn't fail. The patient selection did.

Three trials asked whether we can improve patients who were mostly going to recover. The fourth asked whether we can improve patients who weren't — and the answer changed.

Emad Nour (Nourollahzadeh), MD · SNCC 2026

References

1. Prabhakaran S, et al. 2026 guideline for the early management of patients with acute ischemic stroke: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2026;57:e00-e00. doi:10.1161/STR.0000000000000513. PMID: 41582814.
2. Majidi S, Mehta A, Al-Kasab S, et al. Endovascular thrombectomy in medium and distal vessel occlusions: a focused guideline from the Society of Vascular and Interventional Neurology Guidelines and Practice Standards Committee. *Stroke Vasc Interv Neurol*. 2026;6:e002314.
3. Hu W, Jing X, Chen Z, et al. Endovascular treatment of medium-vessel-occlusion strokes. *N Engl J Med*. 2026;394:1894-1904. doi:10.1056/NEJMoa2514120. PMID: 42127389.
4. Psychogios M, Brehm A, Ribo M, et al. Endovascular treatment for stroke due to occlusion of medium or distal vessels. *N Engl J Med*. 2025;392:1374-1384. doi:10.1056/NEJMoa2408954. PMID: 39908430.
5. Goyal M, Ospel JM, Ganesh A, et al. Endovascular treatment of stroke due to medium-vessel occlusion. *N Engl J Med*. 2025;392:1385-1395. doi:10.1056/NEJMoa2411668. PMID: 39908448.
6. Clarençon F, Bala F, Baptiste A, et al. Mechanical thrombectomy in ischemic stroke with a medium or distal arterial occlusion: the DISCOUNT randomized clinical trial. *JAMA*. 2026. doi:10.1001/jama.2026.8977.
7. 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;11:1065-1069. doi:10.1136/neurintsurg-2018-014678.
8. Ospel JM, Menon BK, Demchuk AM, et al. Clinical course of acute ischemic stroke due to medium vessel occlusion with and without intravenous alteplase treatment. *Stroke*. 2020;51:3232-3240.
9. Anastasiou A, Corbaz H, Christodoulou E, et al. Mechanical thrombectomy and final infarct volume in medium or distal vessel occlusion stroke: a post hoc analysis of a randomized clinical trial. *JAMA Neurol*. 2026;83(6):537-543. doi:10.1001/jamaneurol.2026.0805.
10. Diprose W, Fahed R, Volders D, et al. Reperfusion grade and clinical outcome following medium vessel occlusion thrombectomy in the ESCAPE-MeVO trial. *J Neurointerv Surg*. 2026. doi:10.1136/jnis-2025-024733. PMID: 41651659.
11. Schulze-Zachau V, Rommers N, Dobrocky T, et al. Impact of thrombectomy techniques on outcome in medium or distal vessel occlusion: subanalysis of the DISTAL trial. *J Neurointerv Surg*. 2025. doi:10.1136/jnis-2025-024374.

References — continued

12. Palaodimou L, Safouris A, Papageorgiou NM, et al. Endovascular treatment in acute ischemic stroke due to occlusion of medium or distal vessels: a systematic review and meta-analysis. *Neurology*. 2025;105:e214015. doi:10.1212/WNL.00000000000214015.
13. Jhou HJ, Wang WS, Lee CH, Yang LY, Chen PH. Thrombectomy for distal medium vessel occlusion: a meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2025;14:e042299. doi:10.1161/JAHA.125.042299.
14. Jhou HJ, Lee CH, Tsai YC, Chen PH, Yang LY. Is thrombectomy worth it for isolated posterior cerebral artery occlusion? Meta-analysis and trial sequential analysis. *Stroke Vasc Interv Neurol*. 2024;4:e001084.
15. Chen H, Lakhani DA, Salim HA, et al; MAD-MT Investigators. MAD-MT score: a tool to optimize patient selection for mechanical thrombectomy in distal vessel occlusions. *Stroke*. 2026. doi:10.1161/STROKEAHA.125.054852.
16. Navia P, Barrios AJ, Utrilla C, et al. Middle cerebral artery M2 occlusions: impact of segment dominance and benefit of direct aspiration for the first-pass effect. *J Neuroimaging*. 2025;35:e70019.
17. Virtanen P, Rätty S, Tomppo L, et al. Thrombectomy for medium-sized cerebral vessel occlusion: size does matter. *Eur Stroke J*. 2025. doi:10.1177/23969873251376862.
18. Aziz YN, Aragon Garcia R, Plummer P, et al. Neurointerventional practice change following distal medium vessel occlusion randomized controlled trials: a survey. *Stroke Vasc Interv Neurol*. 2026;6:e001965. PMID: 41503087.
19. Mehta A, Goldman D, Raz E, et al. Should we stop endovascular treatment of M2 occlusions?: a critical look at recent evidence. *Stroke*. 2025. (Special Report)
20. Sporns PB, Almohammad M, Minnerup J, et al. Navigating the distal vasculature: challenges and lessons learned from failed thrombectomy trials. *Interv Neuroradiol*. 2025. doi:10.1177/15910199251365526. PMID: 40808493.
21. Mascitelli JR, De Leacy RA, Mack W, et al. Clinical outcomes and independently adjudicated results of M2 aspiration thrombectomy: a subgroup analysis from the Imperative Trial. *J Neurointerv Surg*. 2025. doi:10.1136/jnis-2025-024023.

References — continued

22. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke: the PROACT II study: a randomized controlled trial. *JAMA*. 1999;282(21):2003-2011. doi:10.1001/jama.282.21.2003. PMID: 10591382.
23. Renú A, Millán M, San Román L, et al. Effect of intra-arterial alteplase vs placebo following successful thrombectomy on functional outcomes in patients with large vessel occlusion acute ischemic stroke: the CHOICE randomized clinical trial. *JAMA*. 2022;327(9):826-835. doi:10.1001/jama.2022.1645.
24. Liu C, Guo C, Li F, et al. Intra-arterial urokinase after endovascular reperfusion for acute ischemic stroke: the POST-UK randomized clinical trial. *JAMA*. 2025;333(7):589-598. doi:10.1001/jama.2024.23480. PMID: 39804674.
25. Hu W, Tao C, Wang L, et al. Intra-arterial tenecteplase after successful endovascular recanalisation in patients with acute posterior circulation arterial occlusion (ATTENTION-IA): multicentre randomised controlled trial. *BMJ*. 2025;388:e080489. doi:10.1136/bmj-2024-080489. PMID: 39809509.
26. Huang J, Yang J, Liu C, et al. Intra-arterial tenecteplase following endovascular reperfusion for large vessel occlusion acute ischemic stroke: the POST-TNK randomized clinical trial. *JAMA*. 2025;333(7):579-588. doi:10.1001/jama.2024.23466. PMID: 39804681.
27. Miao Z, Luo G, Song L, et al. Intra-arterial tenecteplase for acute stroke after successful endovascular therapy: the ANGEL-TNK randomized clinical trial. *JAMA*. 2025;334(7):582-591. doi:10.1001/jama.2025.10800.
28. Hou X, Huang J, Wang L, et al. Intra-arterial tenecteplase after successful reperfusion in large vessel occlusion stroke: a randomized clinical trial. *JAMA Neurol*. 2025;82(9):895-904. doi:10.1001/jamaneurol.2025.2036.
29. Chen W, Yang B, Bai X, et al. Intra-arterial alteplase thrombolysis after successful thrombectomy for acute ischemic stroke in the posterior circulation: the IAT-TOP randomized clinical trial. *JAMA Neurol*. 2026. doi:10.1001/jamaneurol.2026.1074. PMID: 42026933.
30. Li S, Tong X, Zhang H, et al. Occlusion site and outcomes in intra-arterial tenecteplase after successful endovascular therapy: a secondary analysis of the ANGEL-TNK trial. *J Neurointerv Surg*. Published online October 23, 2025. doi:10.1136/jnis-2025-024129. PMID: 41136212.

References — continued

31. Alkhiri A, Alturki F, Alamri AF, et al. Adjunctive intra-arterial thrombolysis after successful endovascular thrombectomy for large vessel occlusion: meta-analysis of outcomes, dosage, and patient selection. *J Neurointerv Surg*. 2025. doi:10.1136/jnis-2025-023404.
32. Salim HA, Pulli B, Yedavalli V, et al. Intra-arterial thrombolytic vs. mechanical thrombectomy in distal medium middle cerebral artery acute ischemic stroke: a preliminary multinational multicenter propensity score-matched study. *Clin Neuroradiol*. 2026. doi:10.1007/s00062-026-01644-6.
33. Zhu Y, Zhang C, Yang H, et al. Endovascular treatment versus standard medical management in primary M3 or M4 occlusion stroke in clinical practice: the oriental-MeVO registry. *BMC Neurol*. 2026;26:510. doi:10.1186/s12883-026-05011-3.
34. Jing X, Chen Z, Zhao Y, et al. Endovascular thrombectomy versus standard medical management in treatment of acute medium vessel occlusion strokes: a multicenter registry. *Radiology*. 2025;317(2):e251040. doi:10.1148/radiol.251040. PMID: 41288486.
35. Zaidi SF, Castonguay AC, Zaidat OO, et al. Safety of adjunctive intraarterial tenecteplase following mechanical thrombectomy: the ALLY pilot trial. *Stroke*. 2025;56(2):355-361. doi:10.1161/STROKEAHA.124.048846. PMID: 39772606.
36. Dassen S, van Es A, Roozenbeek B, et al. Time to endovascular treatment and clinical outcome in acute ischemic stroke with M2-segment occlusion. *J Am Heart Assoc*. 2025;14(22):e043984. doi:10.1161/JAHA.125.043984. PMID: 41220130.
37. Salim HA, Yedavalli V, Lakhani DA, et al. Minimal clinical impact of embolization to new territory on outcomes in medium vessel occlusion strokes treated with mechanical thrombectomy. *J Neurointerv Surg*. 2025;18(1):186-194. doi:10.1136/jnis-2024-022570. PMID: 40044412.
38. Fujiwara S, Uchida K, Ohta T, et al. Impact of intracranial hemorrhage after endovascular treatment for medium vessel occlusion. *Neurosurgery*. 2025;96(4):824-831. doi:10.1227/neu.0000000000003163. PMID: 40085506.
39. 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(5):629-639. doi:10.1002/ana.26331. PMID: 35184327.
40. Guo Y, Wu H, Zhang TY, et al. Endovascular treatment achieves better outcomes than best medical management in patients with M2 occlusion and high stroke severity: a meta-analysis. *J Neurol*. 2023;270(6):2924-2937. doi:10.1007/s00415-023-11653-x. PMID: 36862149.
41. Duloquin G, Graber M, Garnier L, et al. Incidence of acute ischemic stroke with visible arterial occlusion: a population-based study (Dijon Stroke Registry). *Stroke*. 2020;51:2122-2130. doi:10.1161/STROKEAHA.120.029949. PMID: 32486967.
42. Saver JL, Gupta R, Guenego A, et al. Final results of the DISTALS (Distal Ischemic Stroke Treatment With Adjustable Low-Profile Stentriever) randomized trial of Tigertriever 13-EVT for DMVO. *Eur Stroke J*. 2026;11(Suppl 1):i992-i993. doi:10.1093/esj/aakag023.1865. 90-day outcomes presented at ESOC 2026, Maastricht, May 6-8, 2026 (not yet published in full).
43. Fischer U, Brehm A, Ribo M, et al. Endovascular treatment for medium or distal vessel occlusion stroke (DISTAL): 12-month outcomes of a multicentre, open-label, randomised trial. *Lancet Neurol*. 2026;25:571-580. doi:10.1016/S1474-4422(26)00169-9.
44. Almeida LGS, Gonçalves OR, Han ML, et al. General versus non-general anesthesia in endovascular thrombectomy for distal/medium vessel occlusions: a systematic review and meta-analysis. *Clin Neuroradiol*. 2026;36(2):273-284. doi:10.1007/s00062-025-01592-7. PMID: 41288722.
45. Toh KZX, Koh MY, Loh EDW, et al. Distal medium vessel occlusions in acute ischaemic stroke — stent retriever versus direct aspiration: a systematic review and meta-analysis. *Eur Stroke J*. 2023;8(2):434-447. doi:10.1177/23969873231151262. PMID: 37231692.
46. Saver JL, Chapot R, Agid R, et al; Distal Thrombectomy Summit Group. Thrombectomy for distal, medium vessel occlusions: a consensus statement on present knowledge and promising directions. *Stroke*. 2020;51:2872-2884. doi:10.1161/STROKEAHA.120.028956.