



Hôpital du Valais
Spital Wallis

Stroke: acute recanalization

Update 2025

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Service de neurologie

Formation annuelle
de neurologie romande
— Les maladies
cérébrovasculaires





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Actilyse / Tenecteplase

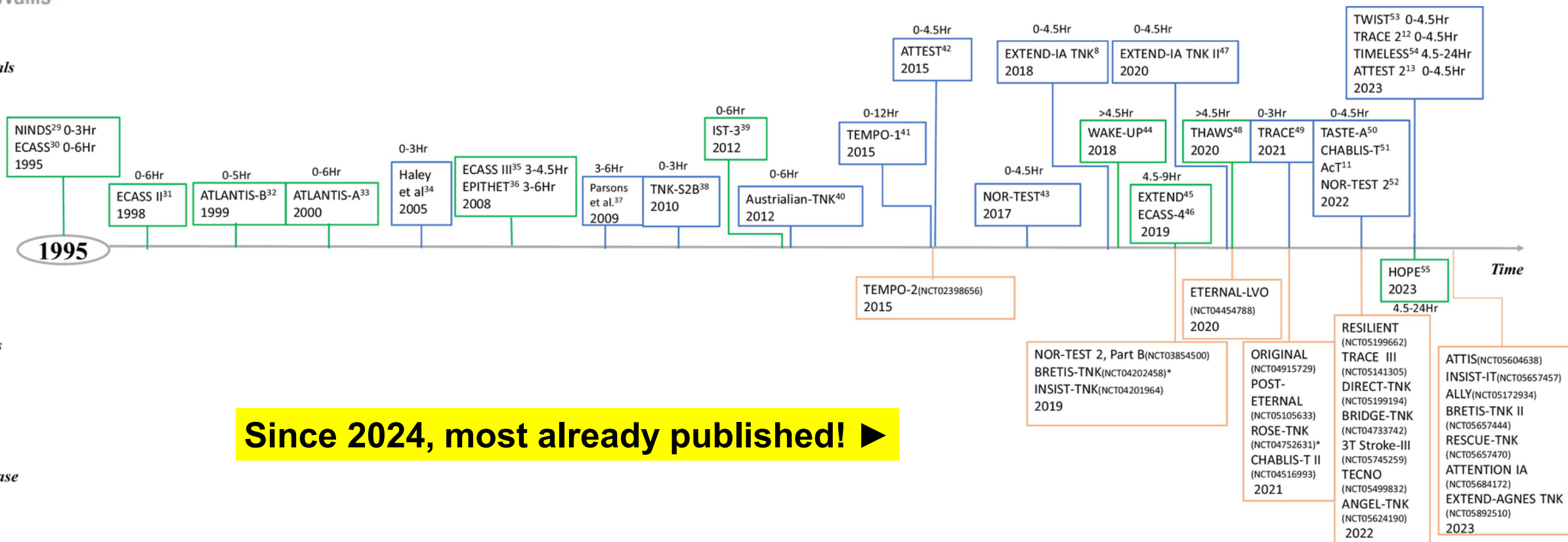
Thrombolysis



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Trials of Alteplase & Tenecteplase (status 04/2024)

Completed Trials





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Thrombolysis < 4.5h → Always without CI

Recommendation

For patients with acute ischaemic stroke of <4.5 h duration, we recommend intravenous thrombolysis with alteplase.

Quality of evidence: **High** ⊕⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

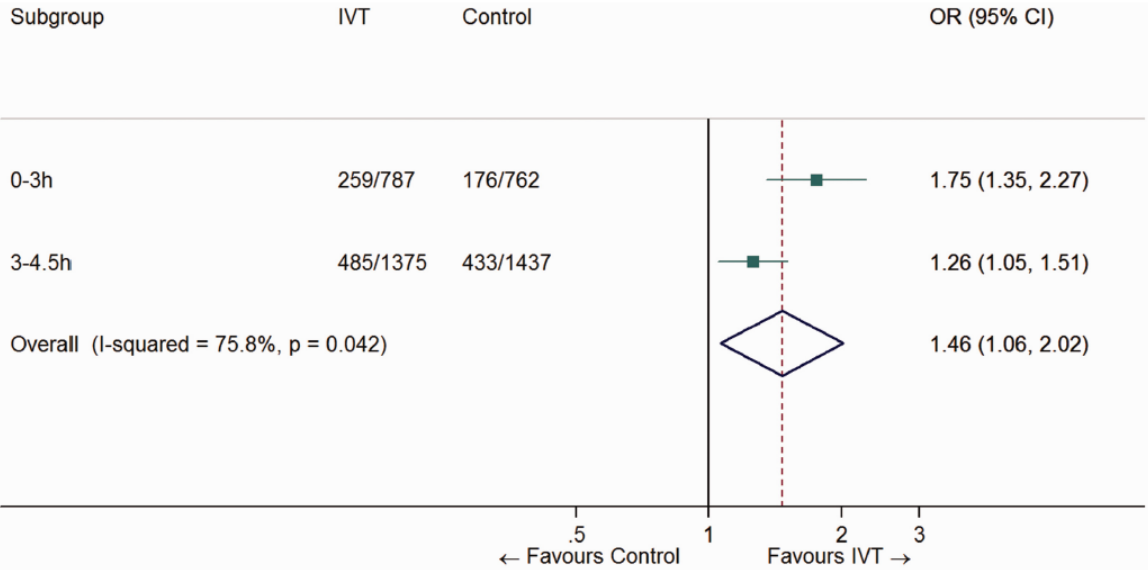
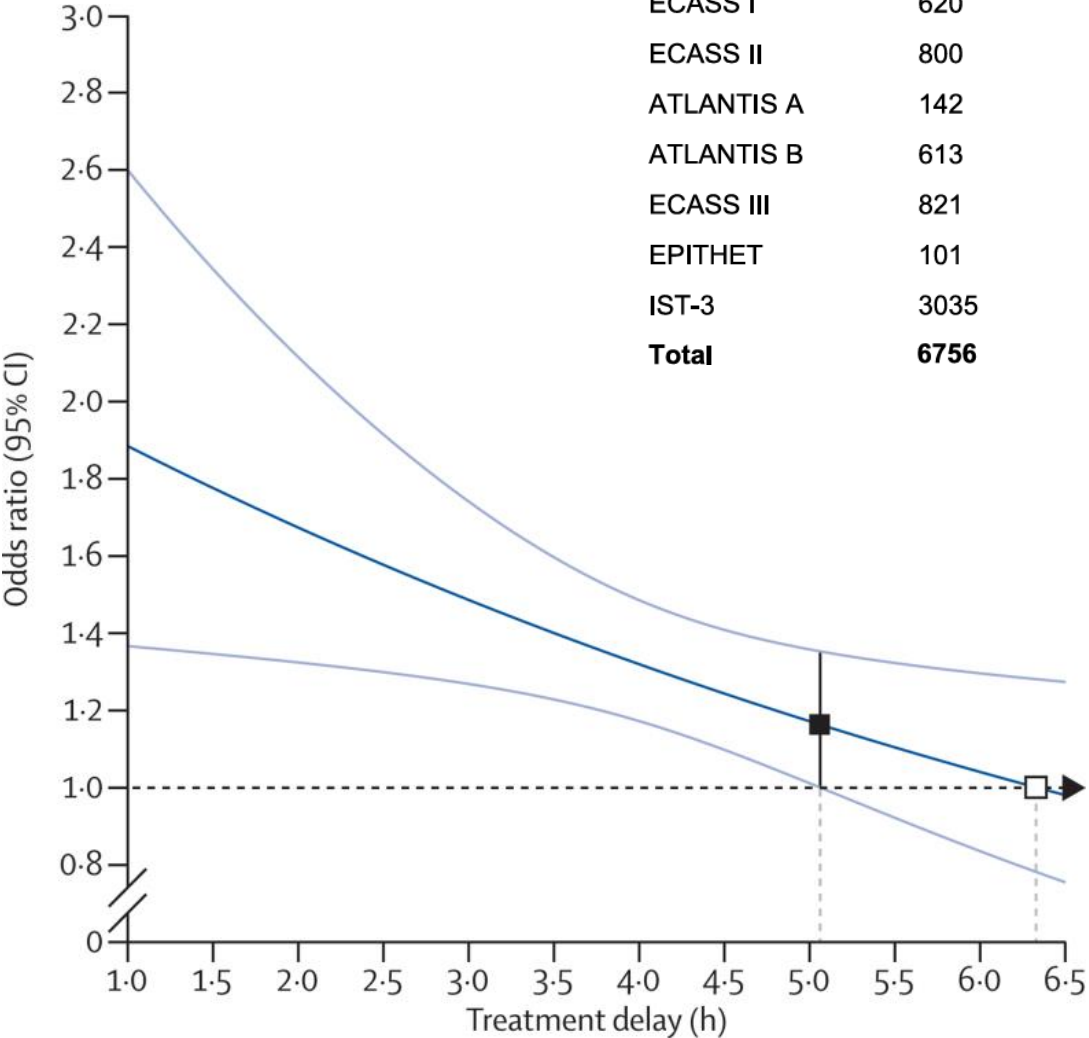


Figure 1. Pooled odds ratio for excellent outcome (mRS 0–1) in patients treated with IVT vs. control in the 0–4.5 h time window. The numbers and the ORs for the two times subgroups are from the individual patient data meta-analysis of nine RCTs by Emberson et al.



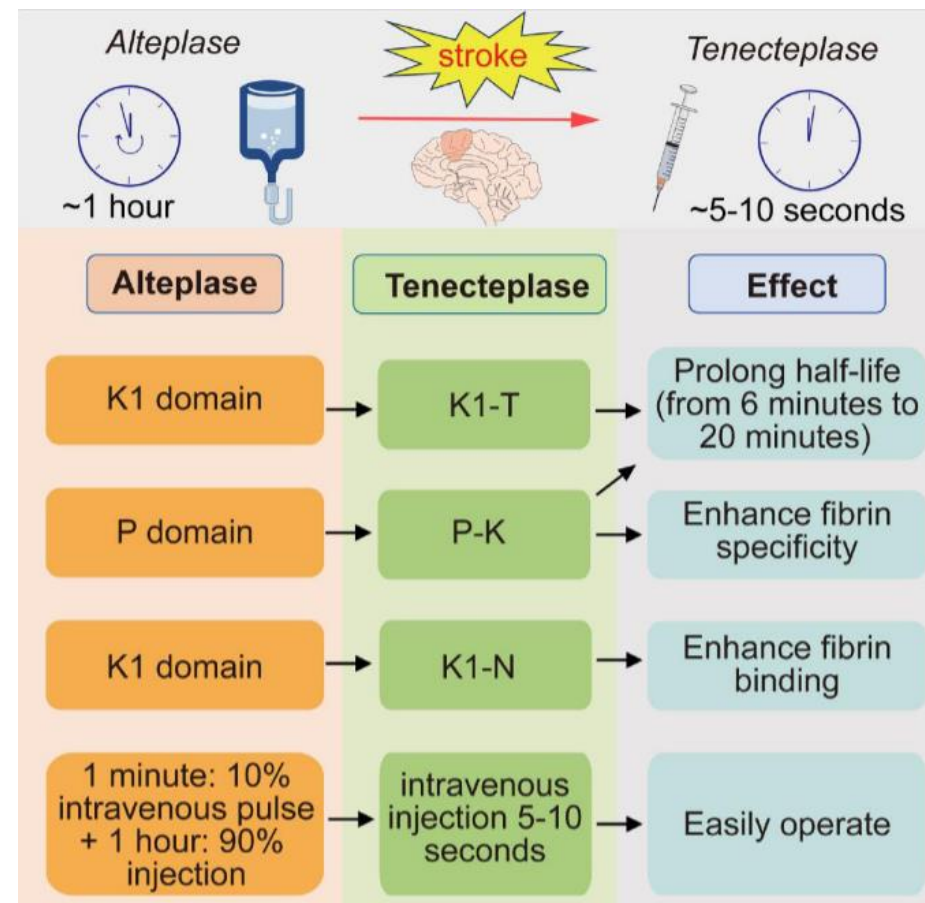
STT trial	Number randomized
NINDS A	291
NINDS B	333
ECASS I	620
ECASS II	800
ATLANTIS A	142
ATLANTIS B	613
ECASS III	821
EPITHET	101
IST-3	3035
Total	6756

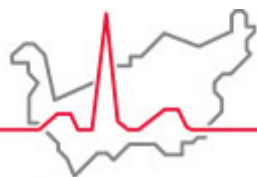


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0.25mg / kg max 25mg (bolus 5-10 sec)

Tenecteplase





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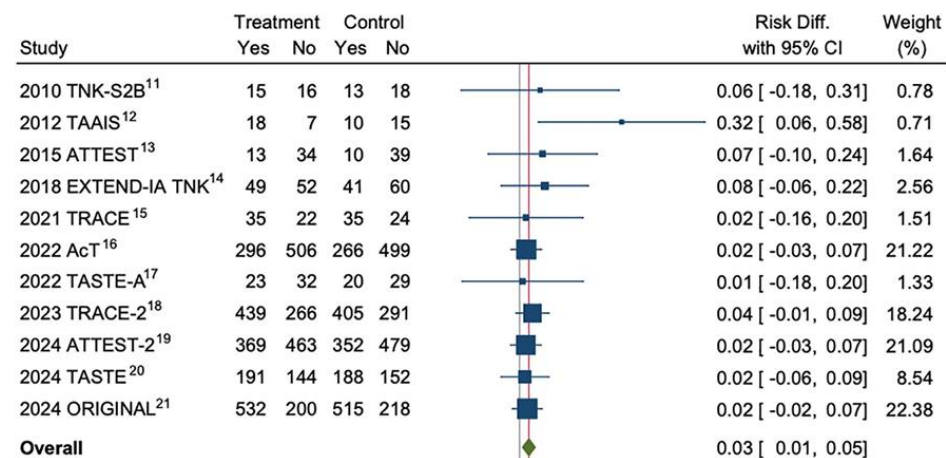
Tenecteplase < 4.5h

Efficacy: TNK $\geq$ ALT

sICH: TNK $\approx$ ALT

Better recanalization before EVT

Figure 1. Meta-analysis of trials comparing tenecteplase 0.25 mg/kg versus alteplase 0–4.5 h after stroke onset for the outcome of modified Rankin Scale 0–1 (no disability) at 90 days.



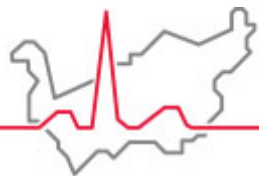
CATALYST-TNK interim analysis indicates non-inferiority of tenecteplase versus alteplase in ischaemic stroke

14 November 2025



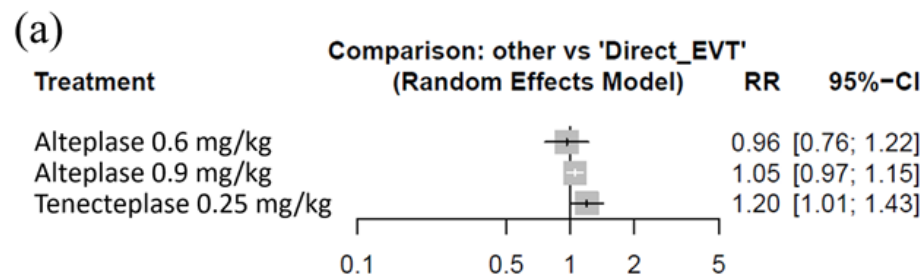
Conclusions

- In unadjusted analyses, IPD meta-analysis confirms non-inferiority of tenecteplase with a non-inferiority margin of <-1.3%
- mRS 0-1 approximately 2.5% in favour of Tenecteplase: in unadjusted analyses including all data (IPD plus ACT, TRACE, TRACE-2) significant for superiority
- mRS distribution favours Tenecteplase but non-significant based on currently available IPD
- No significant difference in mortality or sICH
 - sICH rates low, approximately 2%
- Updated IPD meta-analysis including AcT and TRACE data will offer adjusted analyses and definitive outcome data



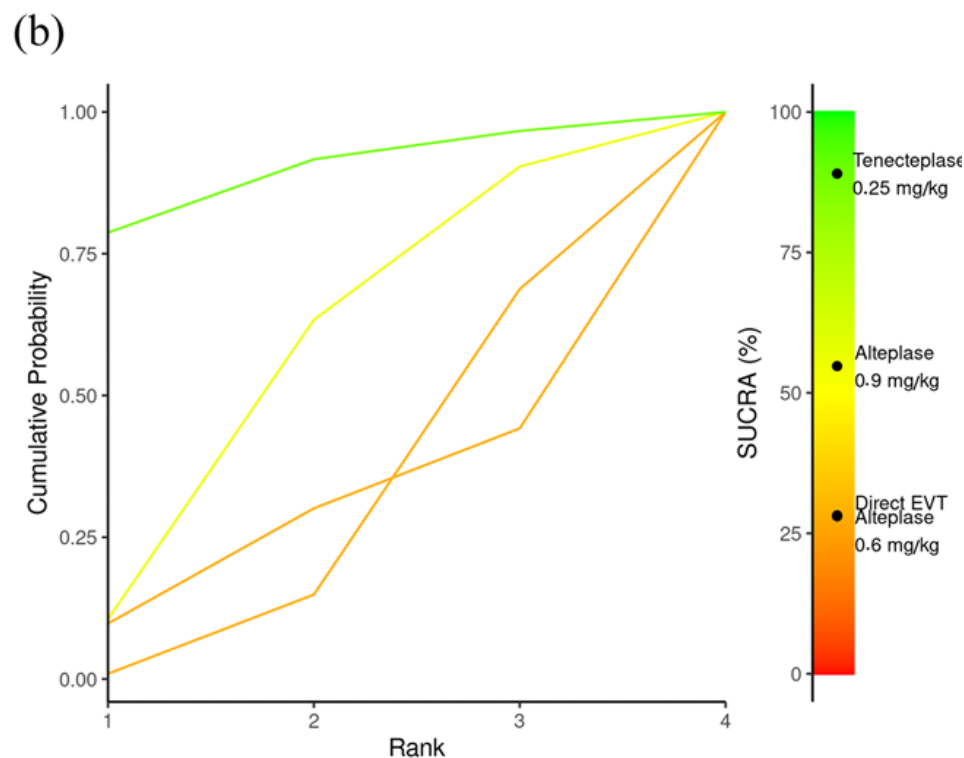
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Which thrombolytic in a Drip & Ship model?



Drip and ship in patients with acute ischemic stroke: a narrative review

Lina Palaiodimou , Nikolaos M. Papageorgiou, Eleni Bakola,



Tenecteplase better before EVT

Recommendation

For patients with acute ischaemic stroke of < 4.5 h duration and with large vessel occlusion who are candidates for mechanical thrombectomy and for whom intravenous thrombolysis is considered before thrombectomy, we suggest intravenous thrombolysis with tenecteplase 0.25 mg/kg over intravenous thrombolysis with alteplase 0.9 mg/kg.

Quality of evidence: Low ⊕⊕

Strength of recommendation: Weak ↑?

Evidence-based Recommendation

PICO1.1 Patients with AIS of <4.5 h duration

For patients with acute ischaemic stroke of <4.5 hrs duration who are eligible for intravenous thrombolysis, **tenecteplase 0.25 mg/kg can be used as a safe and effective alternative to alteplase 0.9 mg/kg.**

Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

Expert Consensus Statement

PICO1.1 Patients with AIS of <4.5 h duration

All MWG members suggest **favouring tenecteplase 0.25 mg/kg** over alteplase 0.9 mg/kg for patients with acute ischaemic stroke of <4.5 hrs duration in light of **safety and efficacy data** and because tenecteplase can be administered with **a single bolus** rather than a 1-hr infusion.

Voting: **9/9 members**

European Stroke Organisation (ESO) expedited recommendation on tenecteplase for acute ischaemic stroke

Trials	N	Design
Act (2022), Phase 3-Canada	1600	AIS<4.5h Non inferiority : -5%
ATTEST (2015) Phase 2b/3-UK	104	AIS <4.5h
TAAIS (2012) Phase 2b- Australia	75	AIS<6H Vessel occlusion-mismatch CT >20%, Tenecteplase 0.10 and 0.25mg/kg, no MT
EXTEND-IA (2018) Phase 2-Australia	202	AIS with LVO eligible to MT
TNK-2S (2010) Phase 2b/3-USA	112	AIS<3h Tenecteplase 0.10 vs 0.25 vs 0.40 mg/kg
TASTE A (2022) Phase 2-Australia	104	AIS<4.5h, MSU
TRACE (2021) Phase 2-China	236	AIS<3h Tenecteplase 0.10 vs 0.25 VS 0.40 mg/kg



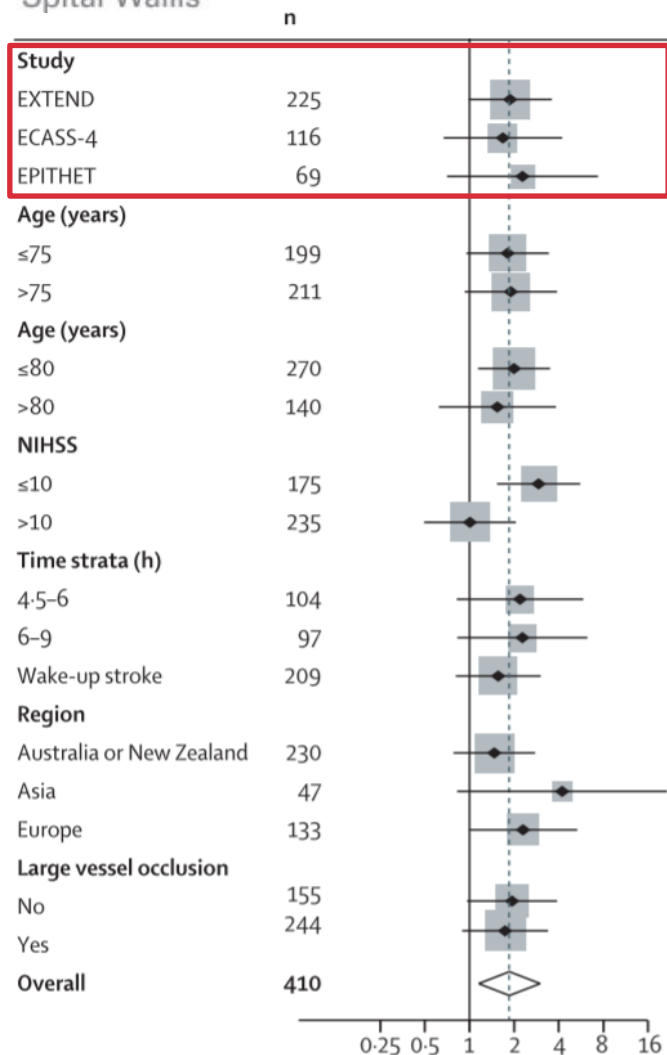
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Thrombolysis 4.5 – 9h and Wake up stroke



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Stroke 4.5 – 9h, unknown onset, perfusion imaging (Alteplase)



Recommendation

For patients with ischaemic stroke of 4.5–9 h duration (known onset time) and with CT or MRI core/perfusion mismatch*, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase.

Quality of evidence: Low ⊕⊕

Strength of recommendation: Strong ↑↑

*In the individual participant data meta-analysis by Campbell et al.,³⁴ core/perfusion mismatch was assessed with an automated processing software and defined as follows:

- Infarct core** volume < 70 ml
- and Critically hypoperfused† volume/Infarct core** volume > 1.2
- and Mismatch volume > 10 ml

MMR > 1.2

** rCBF < 30% (CT perfusion) or ADC < 620 $\mu\text{m}^2/\text{s}$ (Diffusion MRI)

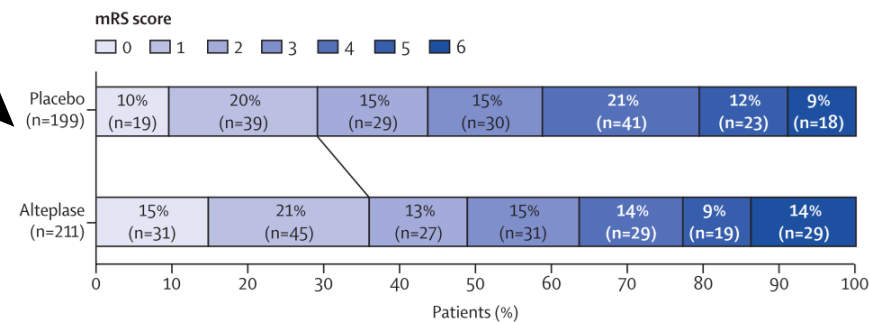
†Tmax > 6 s (perfusion CT or perfusion MRI)

For patients with no CT or MRI core/perfusion mismatch, please see the expert consensus statement below.

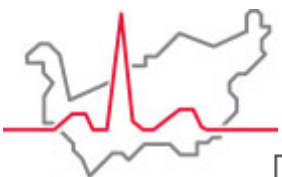
Expert consensus statement

For patients presenting directly to a thrombectomy centre with ischaemic stroke of 4.5–9 h duration (known onset) with CT or MRI core/perfusion mismatch and who are eligible for mechanical thrombectomy, the group members could not reach a consensus regarding whether intravenous thrombolysis should be used before mechanical thrombectomy.

For patients presenting to a non-thrombectomy centre with ischaemic stroke of 4.5–9 h duration (known onset) with CT or MRI core/perfusion mismatch and who are eligible for mechanical thrombectomy, 6 of 9 group members suggest intravenous thrombolysis before mechanical thrombectomy.



↑ sICH (5% vs 1%)



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Study

ECASS-4

EXTEND

THAWS

WAKE-UP

Wake-up stroke (Alteplase)

Recommendation

For patients with acute ischaemic stroke on awakening from sleep, who were last seen well more than 4.5 h earlier, who have MRI DWI-FLAIR mismatch, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase.

Quality of evidence: **High** ⊕⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

For patients with acute ischaemic stroke on awakening from sleep, who have CT or MRI core/perfusion mismatch* within 9 h from the midpoint of sleep, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase.

Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

*In the EOS individual participant data meta-analysis,⁴⁶ core/perfusion mismatch was assessed with an automated processing software and defined as follows:

- Infarct core** volume < 70 ml
- and Critically hypoperfused† volume/Infarct core** volume > 1.2
- and Mismatch volume > 10 ml

MMR > 1.2

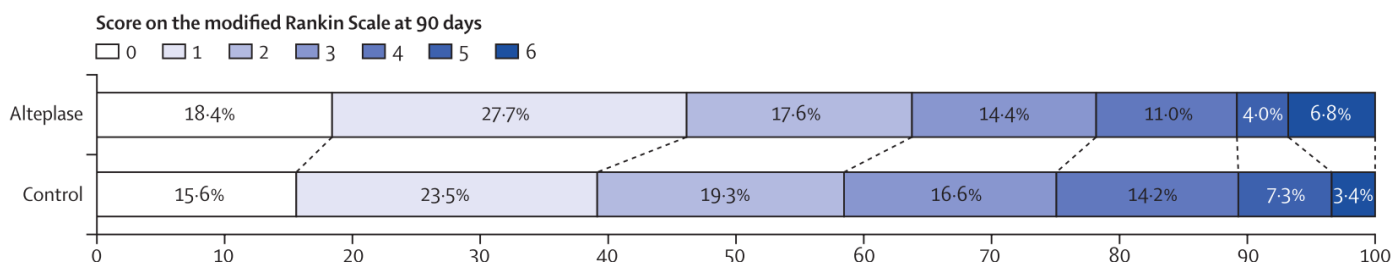
** rCBF < 30% (CT perfusion) or ADC < 620 μm²/s (Diffusion MRI)

† Tmax > 6 s (perfusion CT or perfusion MRI)

Expert consensus statement

For patients presenting directly to a thrombectomy centre with acute ischaemic stroke on awakening from sleep, who would be eligible for both IVT and mechanical thrombectomy, 6 of 9 group members suggest IVT before MT.

For patients presenting to a non-thrombectomy centre with acute ischaemic stroke on awakening from sleep, who would be eligible for both IVT and mechanical thrombectomy, 7 of 9 group members suggest IVT before MT.



↑ sICH (3% vs 1%)



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Neuroimaging: DWI-FLAIR mismatch vs Core/Perfusion mismatch

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IVT with alteplase	no IVT	Relative (95% CI)	Absolute (95% CI)		
DWI-FLAIR mismatch (WAKE-UP trial ³⁹ & EOS Independent participant data meta-analysis ⁴⁶)												
mRS 0–1 at three months												
1	randomised trials	not serious	not serious	not serious	not serious	none	131/246 (53.3%)	102/244 (41.8%)	OR 1.61 (1.09–2.36)*	118 more per 1 000 (from 21 more to 211 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death at three months												
1	randomised trials	not serious	not serious	not serious	not serious	none	10/251 (4.0%)	3/244 (1.2%)	OR 3.38 (0.92–12.52)	28 more per 1 000 (from 1 fewer to 123 more)	⊕⊕⊕⊕ HIGH	CRITICAL
sICH (ECASS 2 definition)												
1	randomised trials	not serious	not serious	not serious	serious ^a	strong association	7/251 (2.8%)	3/244 (1.2%)	OR 2.40 (0.60–9.53)	17 more per 1 000 (from 5 fewer to 94 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Core/Perfusion mismatch (EXTEND, ²⁹ ECASS-4 ³⁰ & EOS ⁴⁶ & Campbell et al. ³⁴)												
mRS 0–1 at three months												
2	randomised trials	not serious	serious ^b	serious	not serious	none	45/112 (40.2%)	29/109 (26.6%)	Adjusted OR 2.14 (1.11–4.12)	171 more per 1 000 (from 21 more to 333 more)	⊕⊕⊕○ MODERATE	CRITICAL
Death at three months												
2	randomised trials	not serious	not serious	not serious ^b	serious ^c	none	14/112 (12.5)	9/109 (8.3)	OR 1.59 (0.66–3.84)	43 more per 1 000 (from 26 fewer to 174 more)	⊕⊕⊕○ MODERATE	CRITICAL

WAKE-UP : Thomalla G (2018) <https://doi.org/10.1056/NEJMoa1804355> ECASS-4 : Ringleb P (2019) <https://doi.org/10.1177/1747493019840938> EOS IPMA : Thomalla G (2020) [https://doi.org/10.1016/S0140-6736\(20\)32163-2](https://doi.org/10.1016/S0140-6736(20)32163-2)
EXTEND : Ma H (2019) <https://doi.org/10.1056/NEJMoa1813046> IPMA : Campbell BCV V (2019) [https://doi.org/10.1016/S0140-6736\(19\)31053-0](https://doi.org/10.1016/S0140-6736(19)31053-0)

Evidence-based Recommendation

PICO 2. AIS of <4.5 h duration -LVO

For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis, we recommend **tenecteplase 0.25 mg/kg over alteplase 0.9 mg/kg**. Intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: Moderate ⊕⊕⊕

Strength of recommendation: Strong ↑↑

Expert Consensus Statement

PICO 2. AIS of <4.5 h duration -LVO

For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis and are **directly admitted to a thrombectomy-capable center**, all MWG members suggest **IVT with tenecteplase 0.25 mg/kg over skipping IVT**. For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis and are admitted to a **center without mechanical thrombectomy capability**, all MWG members suggest **IVT with tenecteplase 0.25mg/kg followed by rapid transfer to a thrombectomy-capable center**.

Voting: **9/9 members**

Pico 3 Wake-up AIS and of unknown onset

Expert Consensus Statement

All MWG members suggest that **tenecteplase 0.25 mg/kg could be a reasonable alternative to alteplase 0.9 mg/kg** for patients with acute ischaemic stroke on awakening from sleep or acute ischemic stroke of unknown onset and who are eligible for intravenous thrombolysis **after selection with advanced imaging** (FLAIR-DWI mismatch or perfusion mismatch as outlined in the 2021 ESO Guidelines on IVT).

Voting: **9/9 members**

Berge E et al, Eur Stroke J 2021; 6: I-LXII



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Late IV thrombolysis 4.5 – 24h (>9h)



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HOPE trial

China

NIHSS 4-26

Pre-mRS 0-1

Perfusion CT

- Core $\leq 70\text{ml}$
- MMR ≥ 1.2
- MM volume $\geq 10\text{ml}$

No / EVT refusal

All vessels included

	Alteplase (n = 186)	Standard medical treatment (n = 186)
Vessel occlusion, No. (%) ^h		
Internal carotid artery	33 (17.7)	39 (21.0)
M1 segment of middle cerebral artery	51 (27.4)	46 (24.7)
Proximal M2 segment of middle cerebral artery	21 (11.3)	26 (14.0)
Distal M2 segment of middle cerebral artery	15 (8.1)	18 (9.7)
Distal middle cerebral artery beyond M2	38 (20.4)	25 (13.4)
Anterior cerebral artery	9 (4.8)	12 (6.5)
Posterior cerebral artery	4 (2.2)	5 (2.7)
Basilar artery	9 (4.8)	8 (4.3)
Vertebral artery	2 (1.1)	1 (0.5)
No definite occlusion	4 (2.2)	6 (3.2)
Endovascular treatment, No. (%)	3 (1.6)	7 (3.8)

Alteplase >4.5h, perfusion imaging, no IVT planned

JAMA[®]

QUESTION Does intravenous alteplase administered 4.5 to 24 hours after acute ischemic stroke onset improve outcomes in patients with salvageable brain tissue and no initial plan for thrombectomy?

CONCLUSION In patients with acute ischemic stroke with salvageable brain tissue identified by perfusion imaging who did not initially receive thrombectomy, intravenous alteplase administered 4.5 to 24 hours after onset provided functional benefit.

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POPULATION

212 Men
160 Women

Adults with ischemic stroke and potentially salvageable tissue on imaging presenting 4.5-24 hours after symptom onset

Median age: 72 years

LOCATION

26
Stroke centers
in China



INTERVENTION



372 Patients randomized

186
Alteplase

Intravenous alteplase at 0.9 mg/kg (maximum 90 mg) with 10% given as a bolus over 1 minute followed by a 60-minute infusion of remaining dose in addition to standard treatment

186
Standard treatment

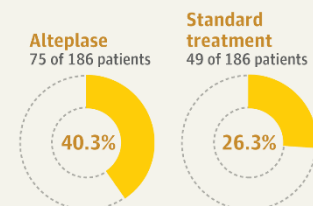
Antiplatelet therapy and supportive care based on established clinical and medical practice guidelines

PRIMARY OUTCOME

Nondisabled functional outcome, defined as modified Rankin Scale score of 0 to 1 at 90 days

FINDINGS

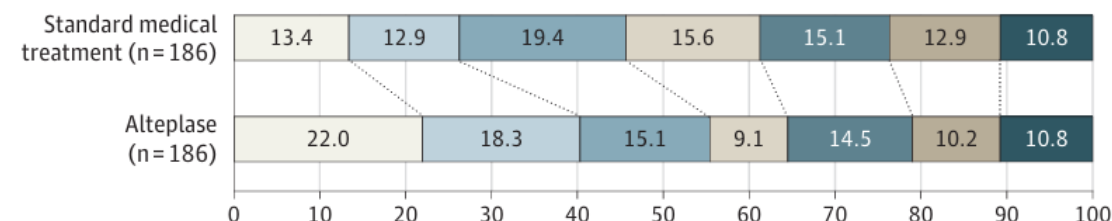
Rate of nondisabled functional outcome



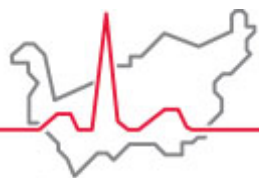
Results were statistically significant:
Adjusted risk ratio, **1.52**
(95% CI, 1.14-2.02); P = .004

Zhou Y, He Y, Campbell BCV, et al; for the HOPE investigators. Alteplase for acute ischemic stroke at 4.5 to 24 hours: the HOPE randomized clinical trial. JAMA. Published online August 7, 2025. doi:10.1001/jama.2025.12063

A Primary analysis



Zhou Y, JAMA 2025, <https://doi.org/10.1001/jama.2025.12063>



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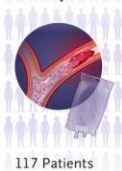
EXPECTS trial

China
NIHSS ≥ 1
Pre-mRS 0-1
Posterior circulation
PC-ASPECT ≥ 7
No / EVT refusal

Patients
• 234 adults
• Median age, 64 years
• Men: 65%; Women: 35%



Alteplase



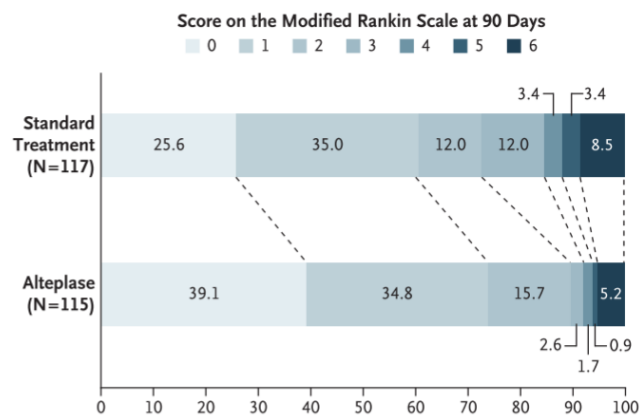
Standard Medical Treatment



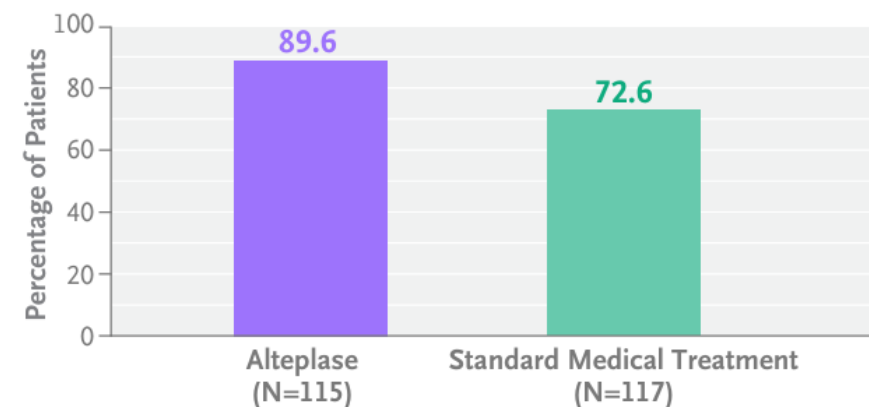
Alteplase $>4.5h$, no IVT planned, *Posterior circulation*

Characteristic	Alteplase (n=117)	Standard Medical Treatment (n=117)
Stroke classification — no. (%)†		
Cardioembolism	12 (10.3)	15 (12.8)
Intracranial atherosclerosis	28 (23.9)	36 (30.8)
Extracranial atherosclerosis	5 (4.3)	6 (5.1)
Small-vessel occlusion	55 (47.0)	40 (34.2)
Undetermined or other etiology	17 (14.5)	20 (17.1)

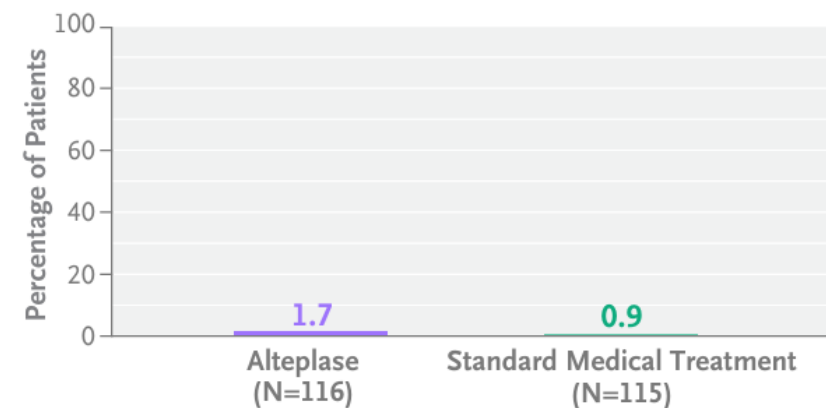
Confirmed large vessel occlusion — no. (%)†		
Proximal posterior cerebral artery	1 (0.9)	5 (4.3)
Basilar artery	6 (5.1)	10 (8.5)
Vertebral artery	14 (12.0)	16 (13.7)



Functional Independence at 90 Days



Symptomatic Intracranial Hemorrhage within 36 Hours



Yan S, N Engl J Med 2025, <https://doi.org/10.1056/NEJMoa2413344>



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TWIST
TRACE-2
TIMELESS
TRACE-III
TEMPO-2
EXIT-BT
CHABLIS-T II
ETERNAL-LVO

Tenecteplase >4.5h, perfusion imaging

- **Meta-analysis of 8 RCT**

- Many Chinese trials

- **NIHSS ≥ 6 (mostly)**

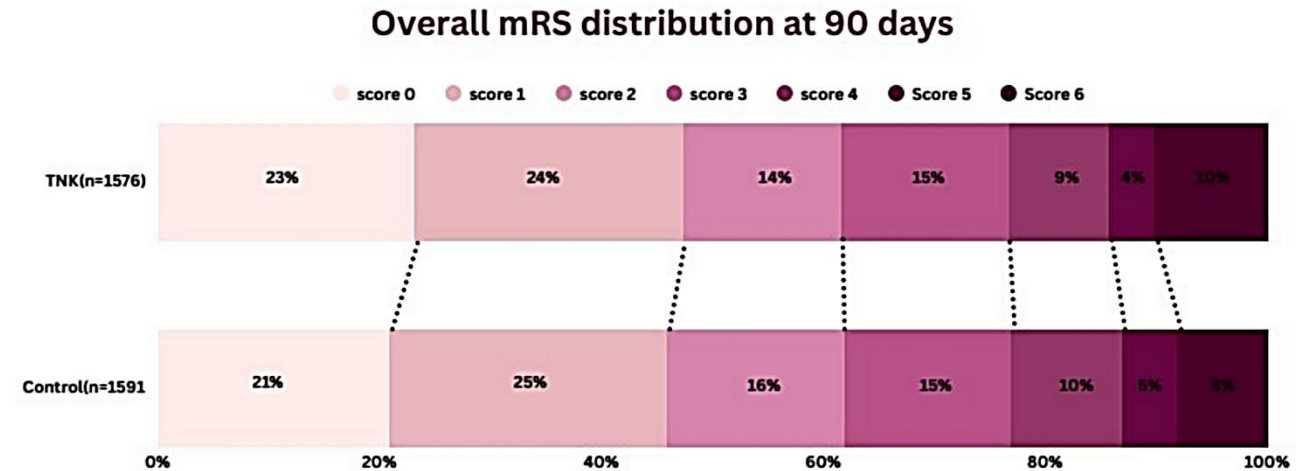
- **LVO y/n, EVT y/n**

- **N=3068**

- **Tenecteplase vs BMT**

- **Results**

- ↑ Early neurological improvement
- ↑ Reperfusion
- No effect on mRS 0-1 outcome, mRS 0-2 slightly better
- No added value when EVT performed
- ↑ sICH



**Perfusion imaging !
(in most studies)**

- Core $\leq 70\text{ml}$
- MMR ≥ 1.8
- MM volume $\geq 15\text{ml}$



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IV thrombolysis under DOAC



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IVT under DOACs

Original Investigation

January 3, 2023

Intravenous Thrombolysis in Patients With Ischemic Stroke and Recent Ingestion of Direct Oral Anticoagulants

Thomas R. Meinel, MD¹; Duncan Wilson, PhD^{2,3}; Henrik Gensicke, MD^{4,5}; et al

Findings In this cohort study including 33 207 patients with ischemic stroke who received intravenous thrombolysis at 64 centers in Europe, Asia, Australia, and New Zealand, the risk of symptomatic intracranial hemorrhage was lower among the 832 patients taking direct oral anticoagulant treatment compared with controls with no anticoagulation. This result was consistent among subgroups and different selection strategies.

Meaning This study found insufficient evidence of excess harm associated with the use of off-label intravenous thrombolysis in selected patients who had taken a direct oral anticoagulant within the previous 48 hours.

Intravenous Thrombolysis in Patients With Recent Intake of Direct Oral Anticoagulants: A Target Trial Analysis and Comparison With Reversal Agent Use



Thomas R. Meinel, MD , Philipp Bücke, MD , Lucio D'Anna, MD , Giovanni Merlino,

	Patients receiving IVT vs not receiving IVT			IVT with vs without prior reversal		
	No IVT	IVT	Adjusted difference (95% CI)	No reversal	Reversal (all idarucizumab)	Adjusted difference, % (95% CI)
N (%)	n=1000	n=342		n=283	n=289	
Safety outcomes, n (%)						
sICH (ECASS III)*	54 (5.9%)	10 (3.0%)	-2.1% (-5.3% to +1.2)	10 (3.7%)	6 (2.1%)	-2.8% (-6.9 to +1.3)
sICH (NINDS)*	55 (6.5%)	9 (3.0%)	-1.1% (-5.2 to +2.9)			
Any radiological ICH*						
None	735 (78.1%)	264 (80.2%)	For any radiological ICH: -3.5% (-9.8 to +2.9)	213 (78.6%)	277 (96.2%)	For any radiological ICH: -16.4% (-22.9 to -10.1)
HI 1	92 (9.8%)	26 (7.9%)		21 (7.7%)	6 (2.1%)	
HI 2	47 (5.0%)	18 (5.5%)		18 (6.6%)	0 (0.0%)	
PH 1	13 (1.4%)	3 (0.9%)		2 (0.7%)	1 (0.3%)	
PH 2	22 (2.3%)	8 (2.4%)		8 (3.0%)	2 (0.7%)	
SAH	27 (2.9%)	9 (2.7%)		8 (3.0%)	2 (0.7%)	
Multiple types	5 (0.5%)	1 (0.3%)		1 (0.4%)	0 (0.0%)	
Any major bleeding†	21 (2.3%)	7 (2.3%)	+0.0% (-2.4 to +2.4)	6 (2.4%)	2 (0.7%)	-0.9% (-2.8 to +1.0)
Orolingual edema†	0 (0.0%)	4 (1.2%)	+1.2% (+0.03 to +2.4)	4 (1.5%)	3 (1.0%)	-0.0% (-1.7 to +1.6)
Mortality (90 d)†	219 (22.7%)	47 (15.7%)	-3.3% (-9.5 to +2.9)	42 (17.1%)	5 (9.3%)	-5.5% (-15.5 to +4.6)
Efficacy outcome, n (%)†						
mRS score of 0–2 or return to baseline (90 d)	405 (43.7%)	181 (62.2%)	+14.4% (+7.1% to +21.8%)	147 (62.0%)	159 (63.9%)	-2.6% (-10.9 to +5.7)
mRS score shift analysis			aOR, 0.60 (0.45 to 0.80)			aOR, 1.32 (0.92 to 1.88)
NIHSS score difference between admission and 24 h	2 (0–7)	3 (1–7)	+0.33 (-0.58 to 1.24)	3 (0–7)	4 (1–9)	+0.05 (-1.2 to +1.2)



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Bridging IVT before EVT



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Bridging IVT before EVT

ALTEPLASE

DEVT

DIRECT-MT

SKIP

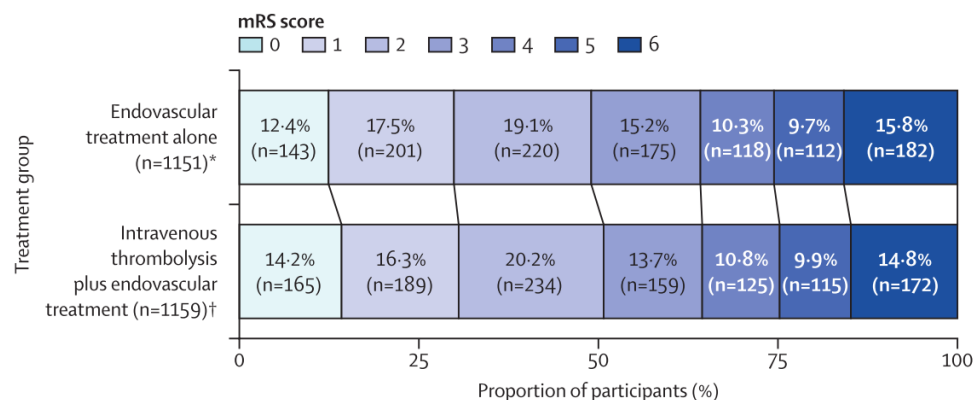
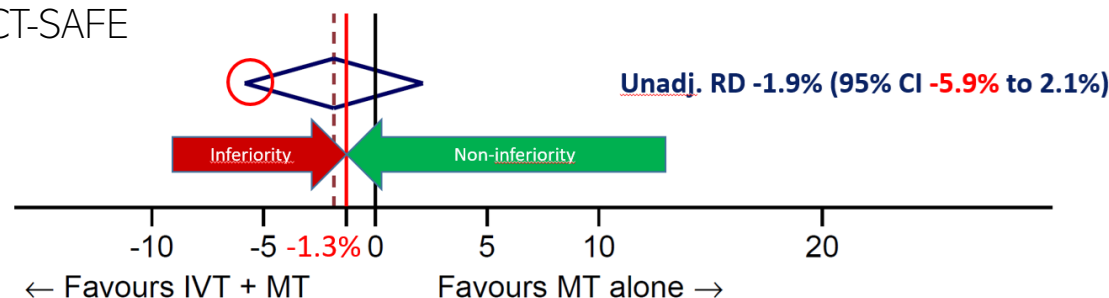
MR CLEAN-NO IV

SWIFT DIRECT

DIRECT-SAFE

Thrombolysis before Thrombectomy in Stroke — A Bridge Not Fallen

Thomas W. Leung, M.D.^{1,2}



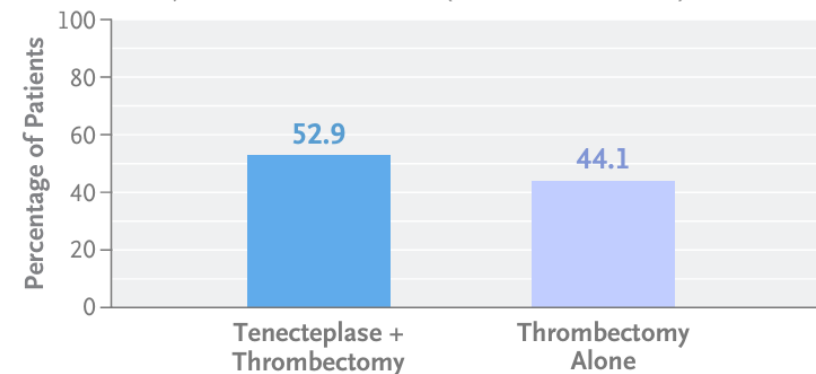
BRIDGE-TNK Trial

ORIGINAL ARTICLE

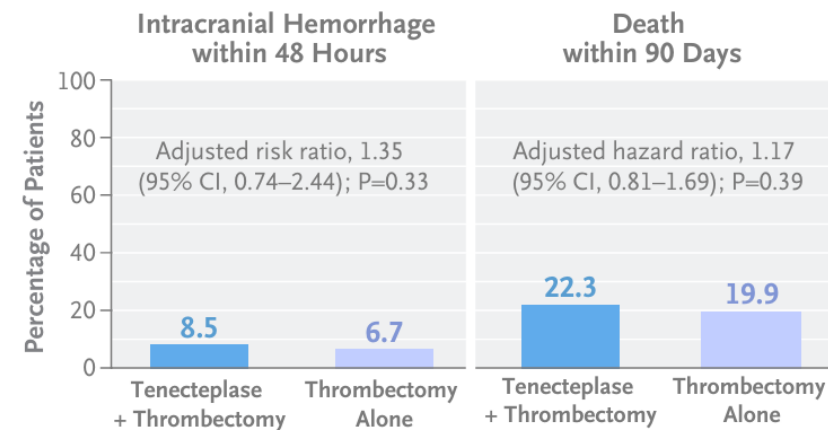
Intravenous Tenecteplase before Thrombectomy in Stroke

Functional Independence at 90 Days

Adjusted risk ratio, 1.18 (95% CI, 1.01–1.39); P=0.04

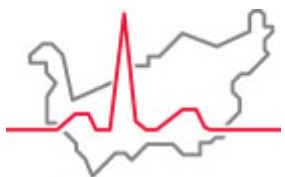


Safety



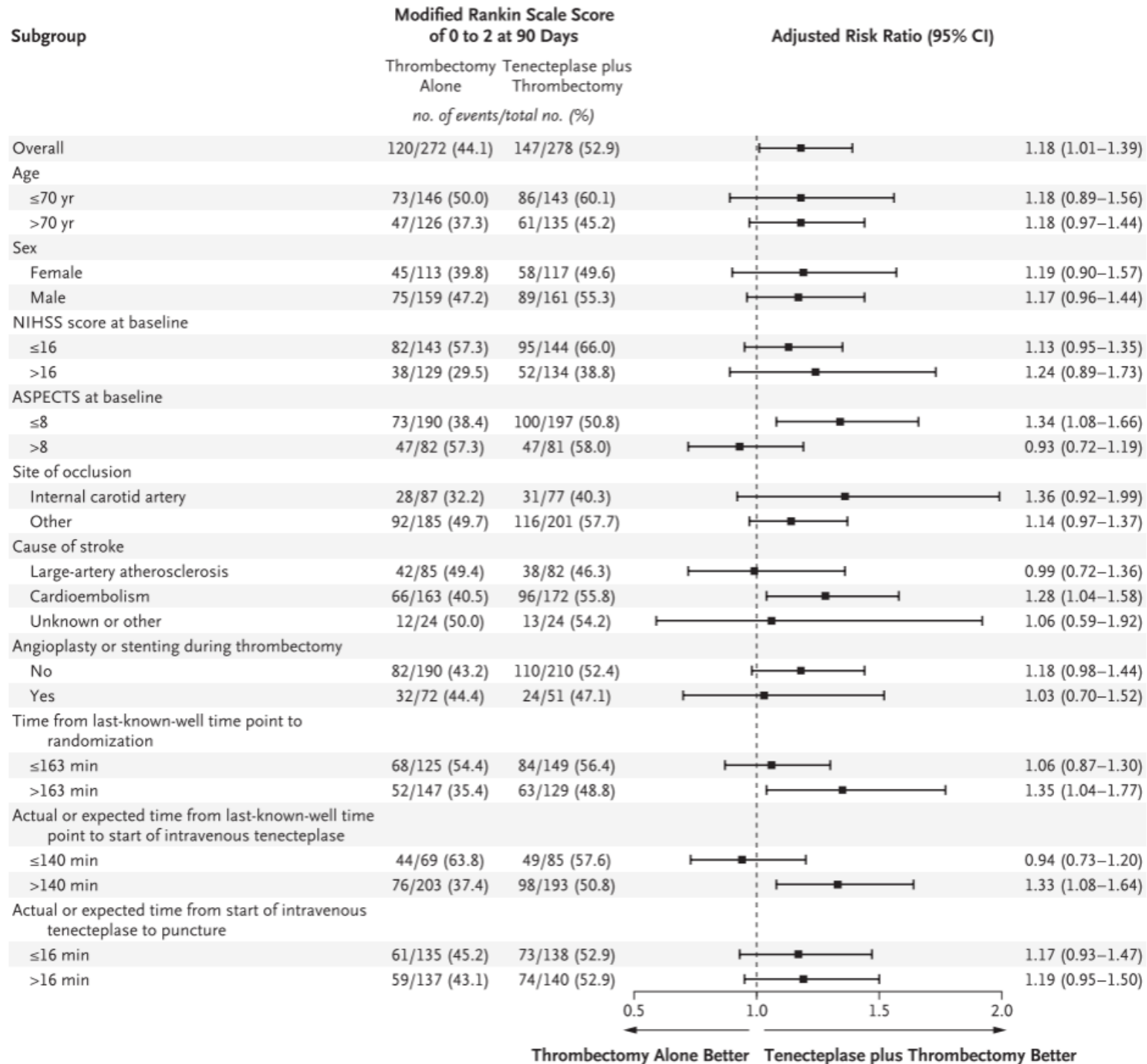
Leung T, N Engl J Med 2025, <https://doi.org/10.1056/NEJMe2506729> / Qiu Z, N Engl J Med 2025, <https://doi.org/10.1056/NEJMoa2503867>

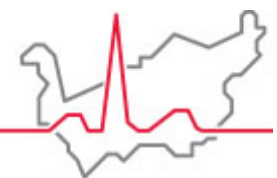
Patel A, Lancet 2023, [https://doi.org/10.1016/S0140-6736\(23\)01142-X](https://doi.org/10.1016/S0140-6736(23)01142-X)



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TENECTEPLASE BRIDGE-TNK Trial





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ALTEPLASE
DEV
DIRECT-MT
SKIP
MR CLEAN-NO IV
SWIFT DIRECT
DIRECT-SAFE

Summary of findings 1. Endovascular thrombectomy with intravenous thrombolysis compared to thrombectomy alone for acute ischaemic stroke

Thrombectomy + IVT compared to thrombectomy alone for acute ischaemic stroke

Patient or population: persons with acute ischaemic stroke

Setting: hospital setting with thrombectomy capability

Intervention: thrombectomy + IVT

Comparison: thrombectomy alone

Time point: within 90 days

No evidence of difference
between MT vs IVT+MT



Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty
	Risk with thrombectomy alone	Risk with thrombectomy + IVT			
Functional independence; assessed with mRS < 3	523 per 1000	539 per 1000 (481 to 596)	RR 1.03 (0.92 to 1.14)	2336 (6 RCTs)	⊕⊕⊕○ Moderate ^a
Excellent functional outcome; assessed with mRS < 2	343 per 1000	340 per 1000 (316 to 360)	RR 0.99 (0.92 to 1.05)	2336 (6 RCTs)	⊕⊕⊕⊕ High
Mortality	160 per 1000	150 per 1000 (124 to 182)	RR 0.94 (0.78 to 1.14)	2336 (6 RCTs)	⊕⊕⊕⊕ High
Asymptomatic intracranial haemorrhage	262 per 1000	297 per 1000 (262 to 339)	RR 1.13 (1.00 to 1.29)	2334 (6 RCTs)	⊕⊕⊕⊕ High
Symptomatic intracranial haemorrhage	47 per 1000	57 per 1000 (40 to 80)	RR 1.20 (0.84 to 1.70)	2336 (6 RCTs)	⊕⊕⊕○ Moderate ^b
Successful revascularisation; assessed with TICI grades 2b to 3	807 per 1000	840 per 1000 (816 to 872)	RR 1.04 (1.01 to 1.08)	2326 (6 RCTs)	⊕⊕⊕⊕ High
Complete revascularisation; assessed with: TICI grade 3	340 per 1000	387 per 1000 (347 to 435)	RR 1.14 (1.02 to 1.28)	2037 (5 RCTs)	⊕⊕⊕⊕ High

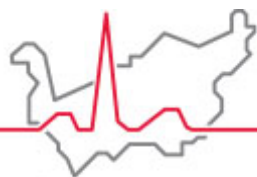
^aThe risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).



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Mechanical thrombectomy (MT)

EVT



EVT for LVO < 8h or WUS (anterior circulation)

TABLE 1 | Landmark studies of EVT for AIS from LVO in the anterior circulation.

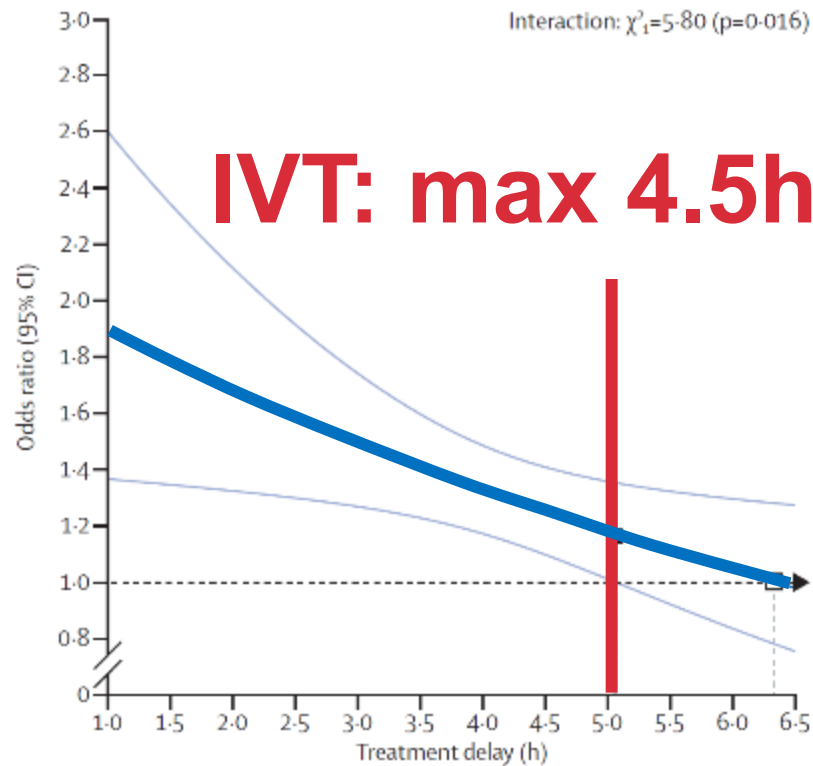
Study	Patient (n)	Key inclusion criteria	Key exclusion criteria	Main imaging modalities	EVT devices
MR CLEAN (13)	233	Age ≥ 18, NIHSS ≥ 2, LVO, IVT < 4.5 h, EVT < 6 h	BP > 185/110 mmHg, coagulopathy, active or recent hemorrhage	CT, CTA, CT perfusion (68%)	Retrievable stent
EXTEND-IA (14)	35	Age ≥ 18, NIHSS ≥ 6, LVO, IVT < 4.5 h, ischemic core < 70 mL, mismatch volume ≥ 10 mL, EVT < 6 h	Intracranial hemorrhage, any terminal illness	CT, CTA, CT perfusion	Solitaire device
ESCAPE (15)	165	Age ≥ 18, NIHSS ≥ 5, LVO, IVT < 4.5 h, small infarct core, EVT < 12 h	ASPECTS 0-5, no or minimal collaterals	CT, CTA	Available thrombectomy device
SWIFT PRIME (16)	98	Age 18–80, NIHSS 8–29, LVO, IVT < 4.5 h, small to moderate infarct core, EVT < 6 h	Hemorrhage, tumor or vacuities on CT or MRI, > 1/3 MCA territory or 100 ml infarct, DWI-ASPECTS ≤ 5	CT, CTA, CT perfusion	Solitaire stent retriever
REVASCAT (17)	103	Age 18–80, NIHSS ≥ 6, LVO, IVT < 4.5 h, EVT < 8 h	Large ischemic core (ASPECTS ≤ 7 on CT or 6 on DWI MRI)	CT, CTA, MRI	Solitaire stent retriever
THERAPY (18)	108	Age 18–85, NIHSS ≥ 8, LVO, ≥ 8 mm clot length	> 1/3 MCA territory infarct, cervical ICA stenosis/occlusion	CT, CTA	Penumbra
THRACE (19)	414	Age 18–80, NIHSS 10-25, LVO, IVT < 4 h, EVT < 5 h	Cervical ICA stenosis/occlusion	CT, CTA, or MRA/MRI	Stent retriever, Penumbra
PISTE (20)	65	Age ≥ 18, NIHSS ≥ 6, LVO, IVT < 4.5 h, EVT < 6 h	Contraindicated for IVT, > 1/3 MCA territory infarct,	CT, CTA	Stent retriever, Penumbra
DAWN (21)	107	Age ≥ 18, NIHSS ≥ 10, LVO, small infarct core (< 1/3 MCA territory), a mismatch between clinical deficit and infarct volume EVT 6–24 h	Rapid improvement in neuro status, active or recent hemorrhage, Coagulopathy	CT, CTA, MRA, CT perfusion, MR perfusion/diffusion	Trevo retriever, Solitaire, or Penumbra
DEFUSE 3 (22)	92	Age 18–85, NIHSS ≥ 6, LVO, ischemic core < 70 ml, mismatch ratio > 1.8, mismatch volume ≥ 15 ml, or DWI volume < 25 ml EVT 6-16 h	BP > 185/110 mmHg, coagulopathy, ASPECTS score < 6 on non-contrast CT	CT perfusion 75%, MR perfusion/diffusion 25%	Trevo retriever



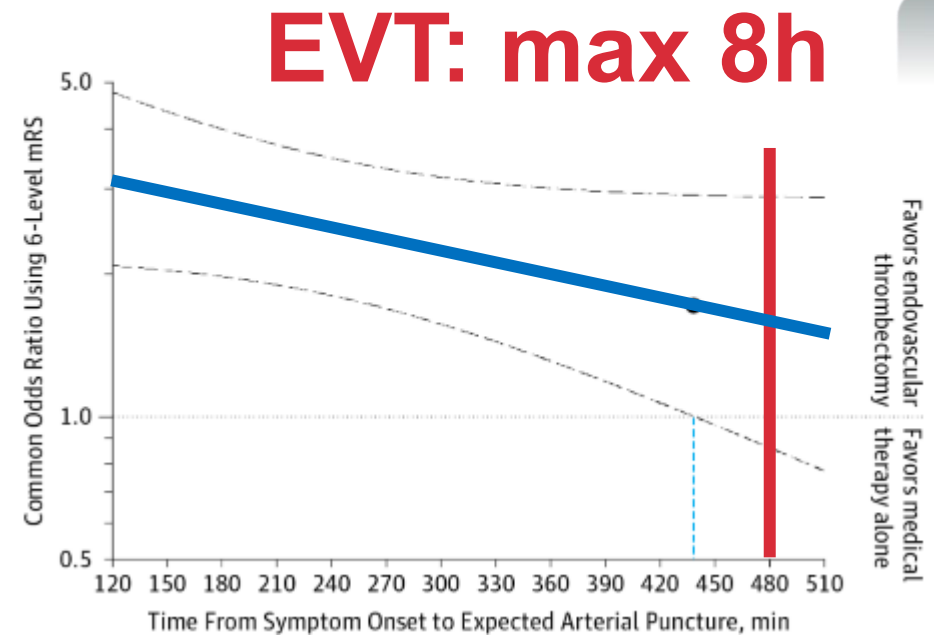
Stroke is an emergency, **act FAST !**

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In most cases, prognostic is time dependent



A Odds ratio for less disability at 3 mo in endovascular thrombectomy vs medical therapy alone groups by time to treatment





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20% of LVO strokes

EVT large cores

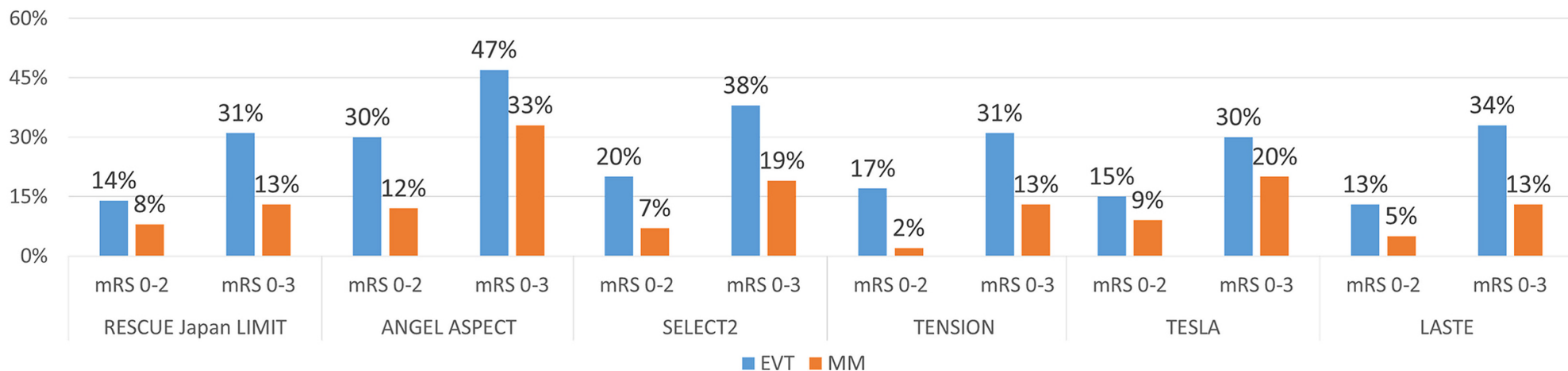
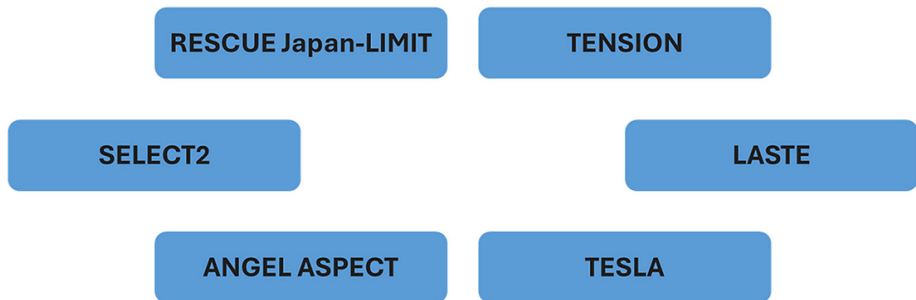
	Anterior circulation LVO	Basilar artery occlusions	Low ASPECT score	Distal occlusions	Low NIHSS score
Image representation					
Current evidence	No EVT EVT	No EVT EVT	No EVT EVT	No EVT EVT	No EVT EVT
Expected evidence (until 2024)	None	Potentially 2 RCTs	Up to 6 RCTs	2-3 RCTs	2 RCTs

Large infarct core trials

Trial	TENSION 	LASTE 	TESLA 	RESCUE-Japan LIMIT 	SELECT 2 	ANGEL-ASPECT 
Official Title	Efficacy and Safety of Thrombectomy in Stroke With Extended Lesion and Extended Time Window	Large Stroke Therapy Evaluation	Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke	Randomized Controlled Trial of Endovascular Therapy for Acute Large Vessel Occlusion With Large Ischemic Core	A Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke	Study of EVT in Acute Anterior Circulation LVO Patients with a large infarCT core
NCT Number	NCT03094715	NCT03811769	NCT03805308	NCT03702413	NCT03876457	NCT04551664
NO.	714	450	300	200	560	502
Country	Austria, Canada, Czechia, Denmark, France, Germany, Norway, Slovakia, Spain	USA, EUROPE	United States	Japan	United States (Canada, Europe)	China
Imaging inclusion Criteria	NCCT or DWI ASPECTS 3-5	NCCT or DWI ASPECTS 0-5 (4-5 >80y)	NCCT ASPECTS 2-5	CT or DWI ASPECTS 3-5	1.ASPECTS ≥6 & core ≥50cc 2.ASPECTS 3-5 & core ≥50cc 3.ASPECTS 3-5 & core <50cc	1.ASPECTS 3-5 2.ASPECTS >5(>6h): core 70-100cc 3.ASPECTS <3: core 70-100cc
NIHSS	<26	NIHSS >5	NIHSS >6	NIHSS ≥6	NIHSS ≥6	NIHSS 6-30
Age	>18	≥18	18-85	>18	18-85	18-80
Time	< 12h LSW	< 6.5h LKW	Random < 24h	Random < 6h LKW , 6-24h FLAIR(-)	Treat < 24h (0-12 vs 6-24)	Random < 24h
Primary Outcome	mRS shift analysis	mRS 90d & 180d	Utility-weighted 90d mRS	mRS 0-3 90d	shift on 90d mRS	mRS 90d
Actual Study Start Date	2018.7.20	2019.04.07	2019.7.16	2018.11	2019.10.11	2020.9.28
Estimated Primary Completion Date	2020.8.31	2021.12	2022.7.16	Published (NEJM)	2021.5.1	2022.11

Core : [rCBF<30%] on CTP or [ADC<620] ; Information source : <https://clinicaltrials.gov> and website

Mechanical Thrombectomy for Large Ischemic Stroke: A Critical Appraisal of Evidence from Six Randomized Controlled Trials



	ASPECTS 3-5	CT ASPECTS 0-2	DWI ASPECTS 0-2	Absence of perfusion mismatch	Ischemic core up to 150ml	Ischemic core >150ml	Elderly(≥80y)
Early Window (0-6 hours)							
Late Window (6-24 hours)							

- Sufficient evidence (significant EVT treatment effect from two or more clinical trials)
- Likely evidence (significant EVT treatment effect from one clinical trial, without evidence of significant heterogeneity or harm)
- Limited evidence, pooled analysis needed
- Absence of evidence, unlikely to be clarified using pooled analysis

ATLAS meta-analysis consolidates EVT's efficacy in large-core stroke with benefits seen across majority of patient subgroups

31 October 2025



Results

Primary Outcome - Shift analysis: aGenOR: 1.63, 95% CI: 1.42 to 1.87, $p < 0.001$
 mRS 0-2: EVT: 19.5% vs MM: 7.5%, aRR: 2.61, 95% CI: 2.03 to 3.54, $p < 0.001$
 mRS 0-3: EVT: 36.6% vs MM: 19.8%, aRR: 1.95, 95% CI: 1.60 to 2.38, $p < 0.001$
 Mortality: EVT: 31% vs MM: 37%, aRR: 0.82, 95% CI: 0.70 to 0.97, $p = 0.018$



worldstrokecongress.org

ONE WORLD VOICE FOR STROKE

Safety Outcomes

sICH: EVT: 5.5% vs MM: 2.7%, aRR: 2.02, 95% CI: 1.13 to 3.59, $p = 0.017^*$
 Neurological Worsening: EVT: 22% vs MM: 17%, aRR: 1.27, 95% CI: 0.94 to 1.71, $p = 0.123$
 Mortality: EVT: 31% vs MM: 37%, aRR: 0.82, 95% CI: 0.70 to 0.97, $p = 0.018$

Conclusions 2

- EVT treatment effect was maintained across key clinical and imaging subgroups - age, sex, clinical severity, time to thrombectomy and stroke size
- EVT maintained consistent treatment effect in ASPECTS < 6, including very low ASPECTS (0-2), at least within the early time window
 - Absolute proportion of patients with functional independence and independent ambulation was reduced
- EVT maintained consistent treatment benefit in patients with core volume 100-150mL
- These results establish the superiority of endovascular thrombectomy over best medical management in this population that accounts for ~1/5th of LVO patients

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ONE WORLD VOICE



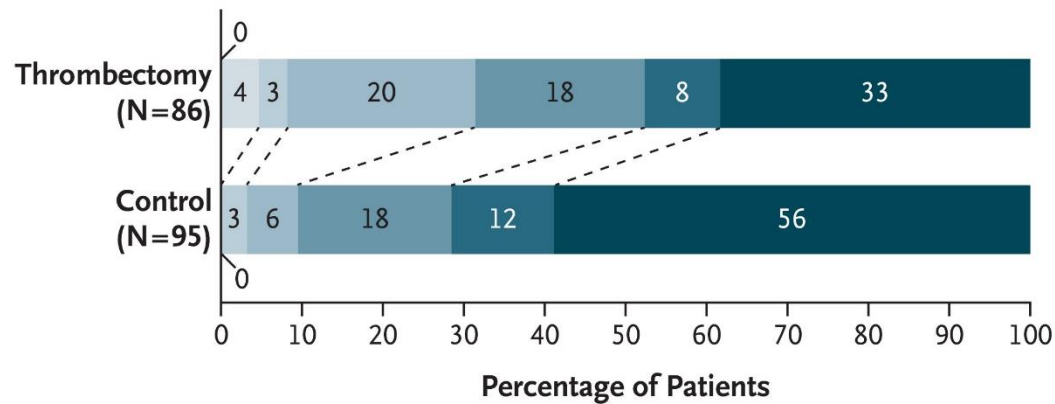
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LASTE

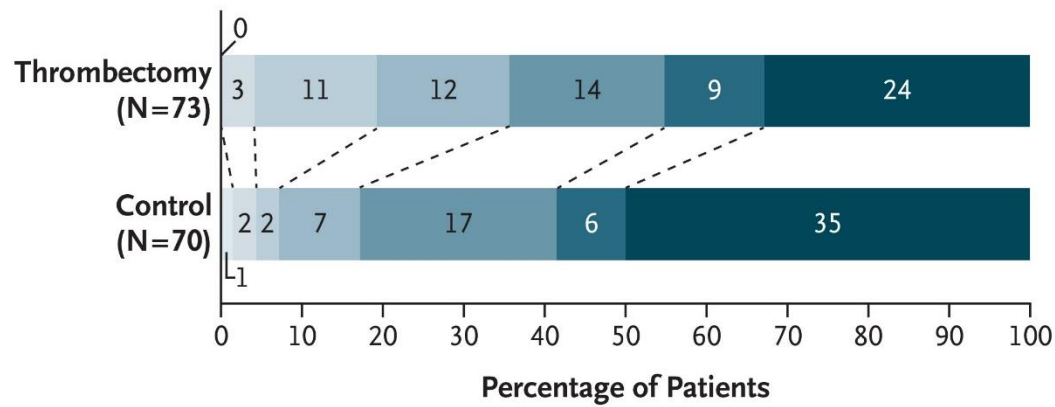
Low ASPECT (0-2) remains a critical condition!

Score on the Modified Rankin Scale: 0 1 2 3 4 5 6

B Patients with Baseline ASPECTS Value ≤ 2



C Patients with Baseline ASPECTS Value ≥ 3



Need for better selection!

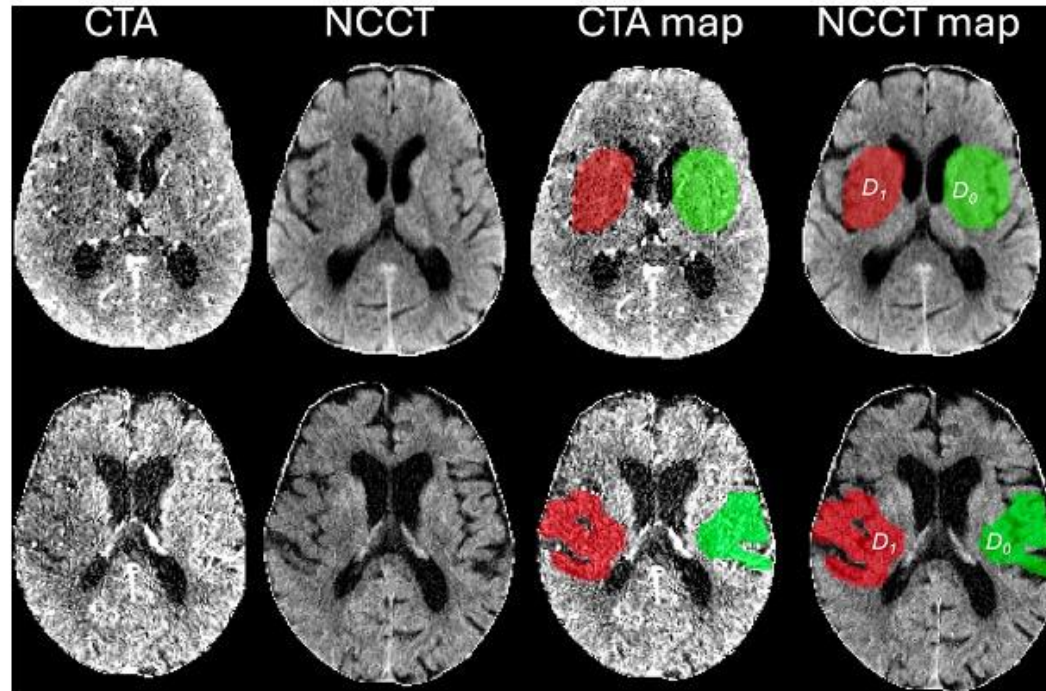
mRS 4-6 = 59% !

mRS 4-6 = 86% !

«Salvage of penumbral brain tissue represents one mechanism underlying the benefit of thrombectomy».

Li M, NEJM 2024

Net Water Uptake at CT Predicts the Treatment Effect of Thrombectomy for Low ASPECTS Stroke



- Secondary analysis of patients with large ischemic lesions (TENSION Trial)
- Net water uptake (NWU) on admission CT predicted worse outcomes (OR 0.33)
- Endovascular therapy was more efficacious in patients with low NWU (<15%)

Broocks G et al. Published: November 4, 2025
<https://doi.org/10.1148/radiol.250708>

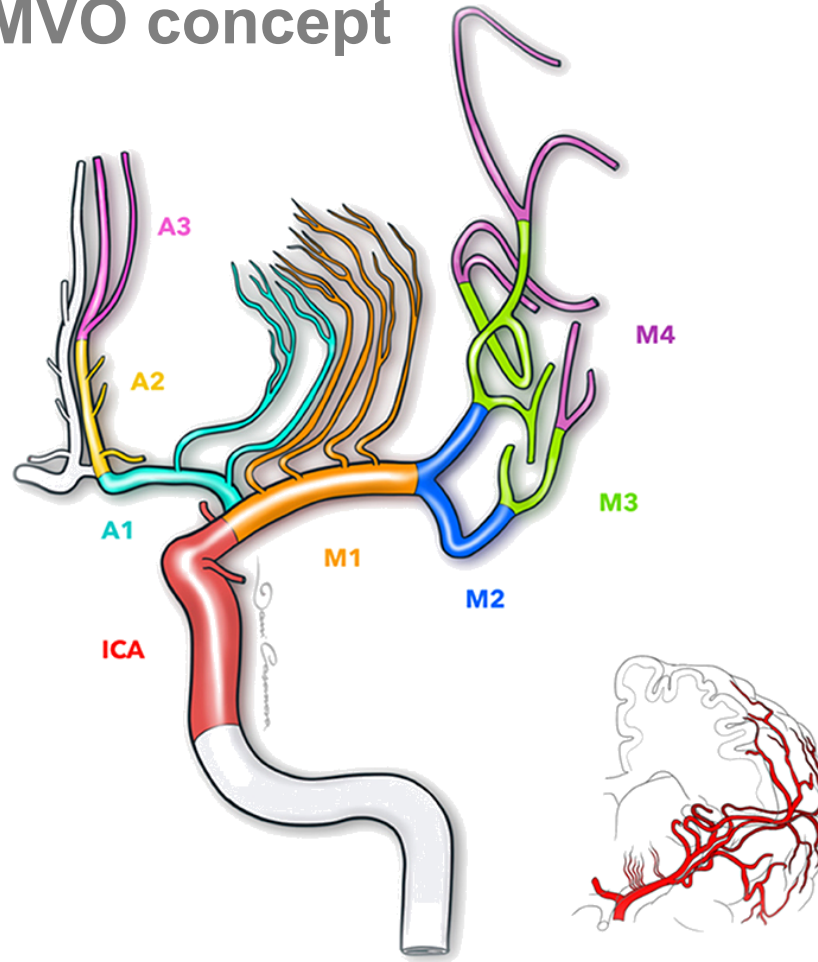
Radiology



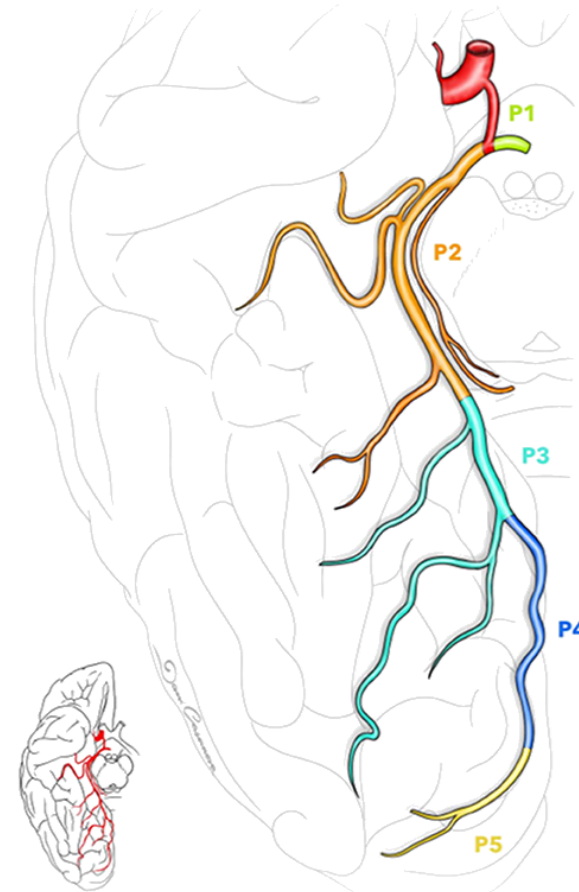
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EVT for DMVOs

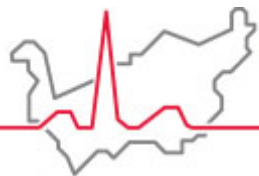
DMVO concept



	M2	M3	M4	A1	A2	A3
DISTAL	x	x	x	x	x	x
DISCOUNT	x*	x		x	x	x
ESCAPE-MeVO	x	x			x	x
DISTALS	x	x		x	x	x



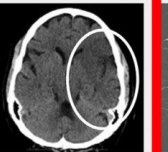
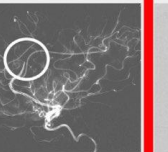
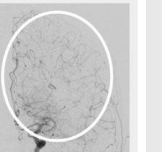
	P1	P2	P3
DISTAL	x	x	x
DISCOUNT	x	x	x
ESCAPE-MeVO		x	x
DISTALS	x	x	x



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DISTAL  
ESCAPE MeVO 
DISCOUNT 
DISTALS 
DUSK 

EVT for DMVOs

	Anterior circulation LVO	Basilar artery occlusions	Low ASPECT score	Distal occlusions	Low NIHSS score
Image representation					
Current evidence					
Expected evidence (until 2024)	None	Potentially 2 RCTs	Up to 6 RCTs	2-3 RCTs	2 RCTs

MeVO: the next frontier?

Mayank Goyal ^{1,2} Johanna Maria Ospel ^{1,3} Bijoy K Menon,^{1,2}
Michael D Hill ^{1,2}

As several randomized trials have shown the overwhelming benefit of endovascular treatment (EVT) compared with medical management alone for acute ischemic stroke (AIS) due to large vessel occlusion (LVO),¹ EVT has become an integral part of LVO treatment.² For medium vessel occlusions (MeVOs)—that is, M2/, A2/3, and P2/3 segment occlusions—the situation is less clear.

EVT in M2 occlusions from the HERMES collaboration, but these data are not sufficient to change treatment guidelines. At present, such a change requires high level evidence from one, or ideally several, randomized controlled trials.

THE CHALLENGE OF DEFINING MEVOS
Even for LVOs, it is not entirely clear how they should be defined.⁸ Varying criteria

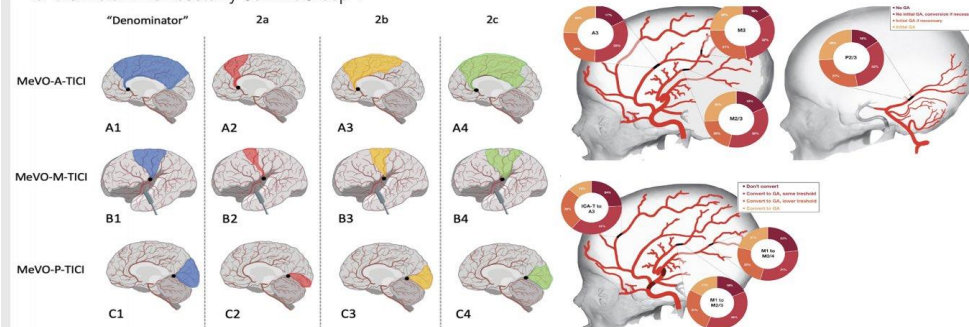


SPECIAL REPORT

Thrombectomy for Distal, Medium Vessel Occlusions

A Consensus Statement on Present Knowledge and Promising Directions

Jeffrey L. Saver, MD; Rene Chapot, MD; Ronit Agid, MD; Ameer Hassan, DO; Ashutosh P. Jadhav, MD; David S. Liebeskind, MD; Kyriakos Lobotesis, MD; Dan Meila , MD; Lukas Meyer, MD; Guy Raphaeli, MD; Rishi Gupta, MD; for the Distal Thrombectomy Summit Group*†



✓ **DISTAL** NCT05029414

Marios-Nikos Psychogios
University Hospital, Basel, Switzerland
Urs Fischer, Prof.Dr.
Bern University Hospital

✓ **ESCAPE – MeVO** NCT05151172

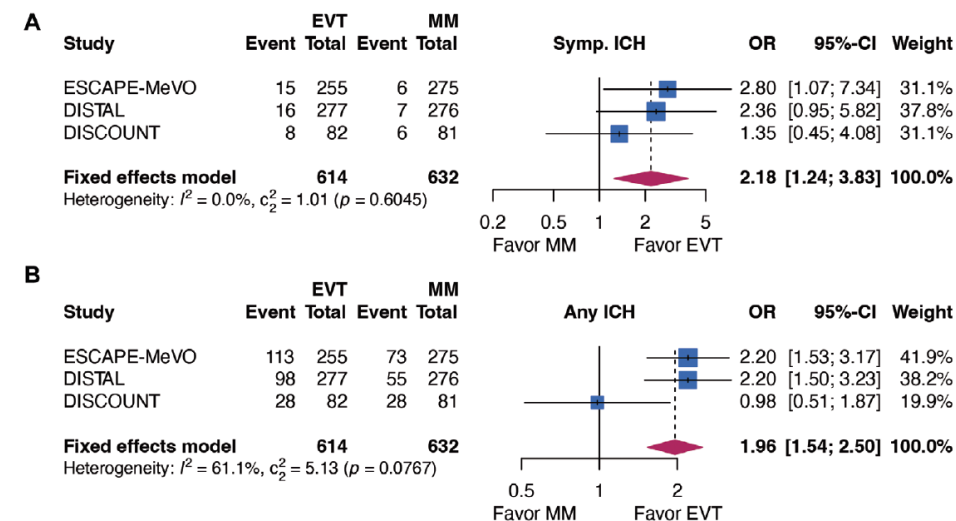
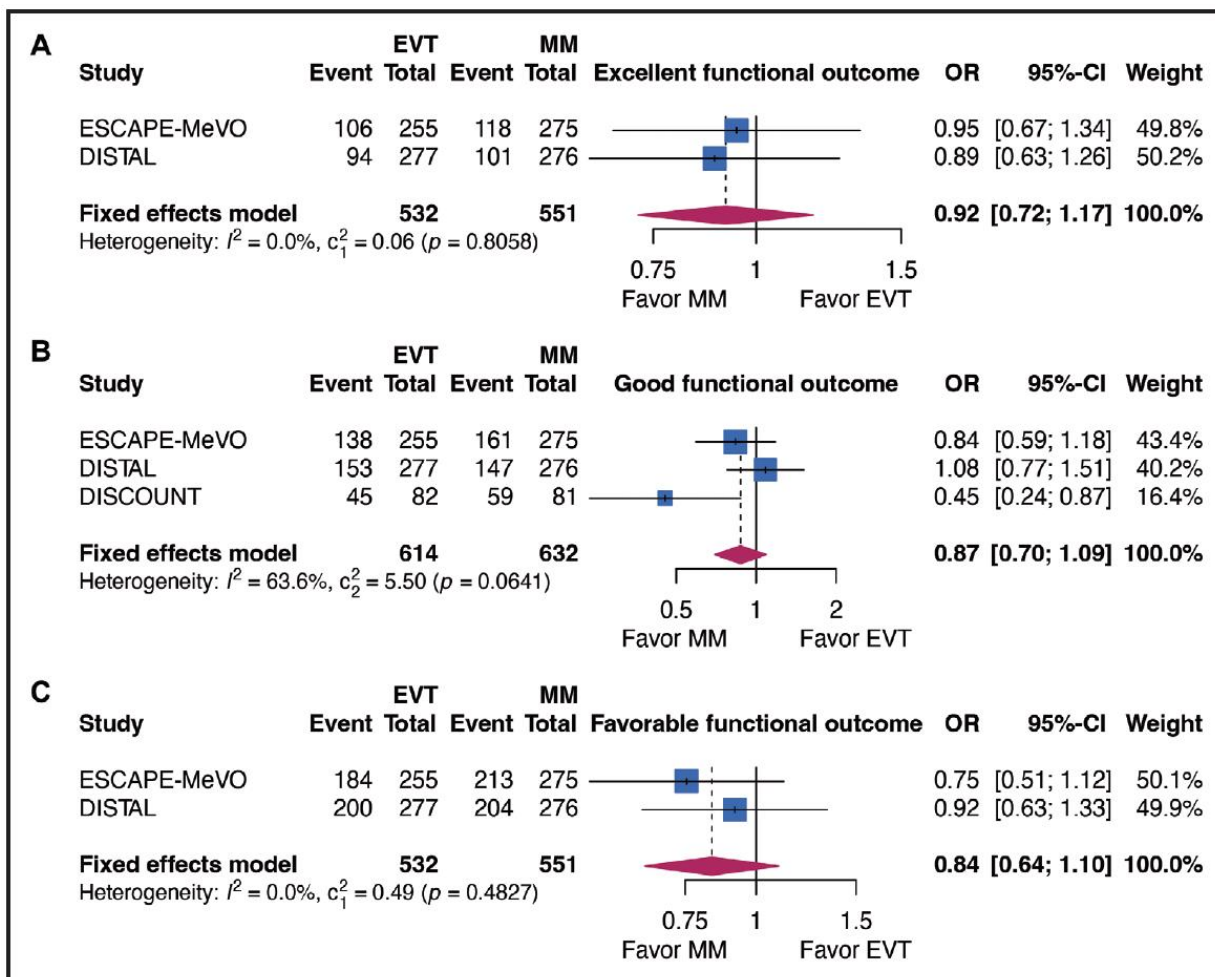
Mayank Goyal
University of Calgary and Foothills Medical Centre

✓ **DISCOUNT** NCT05030142
Frédéric Clarençon, APHP



MeVO
Medium Vessel Occlusion

Thrombectomy for Distal Medium Vessel Occlusion: A Meta-Analysis of Randomized Controlled Trials



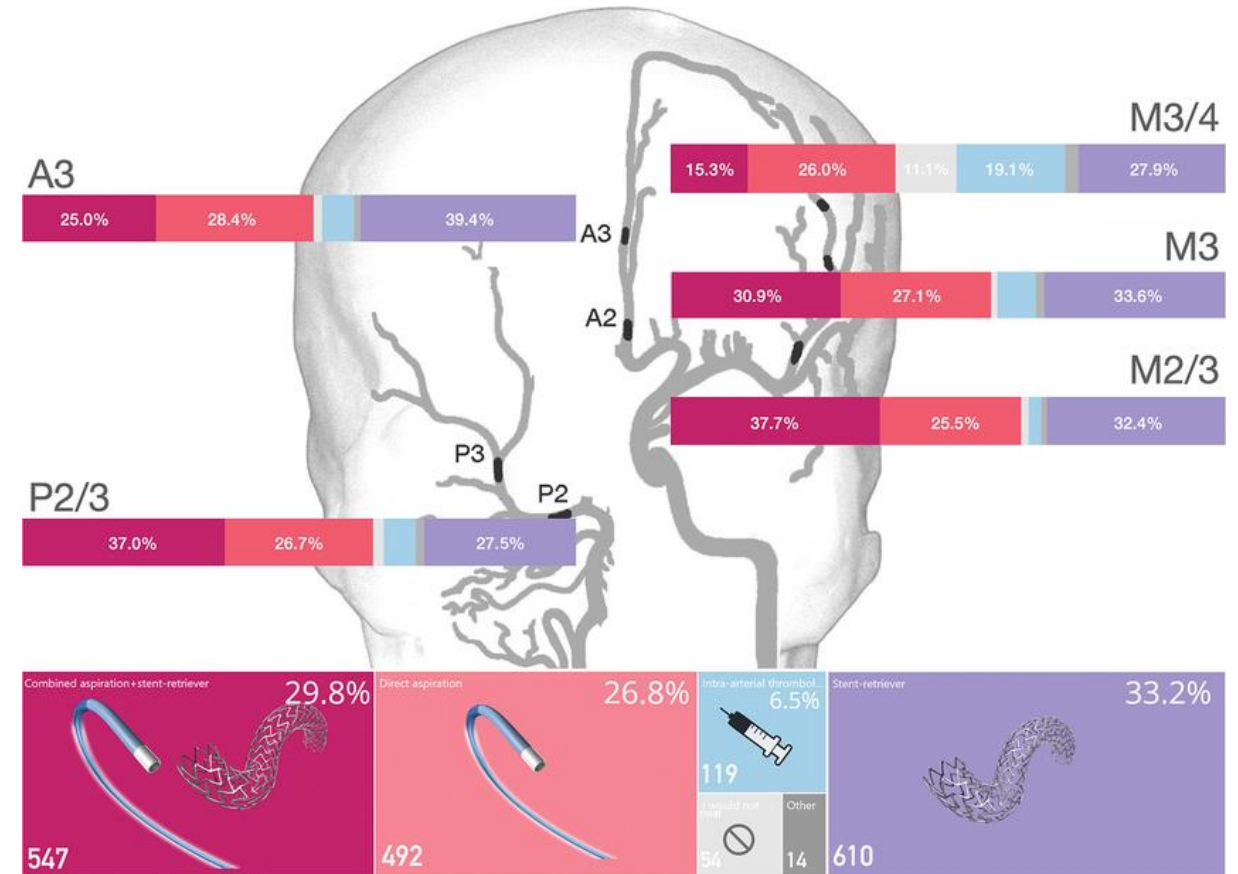
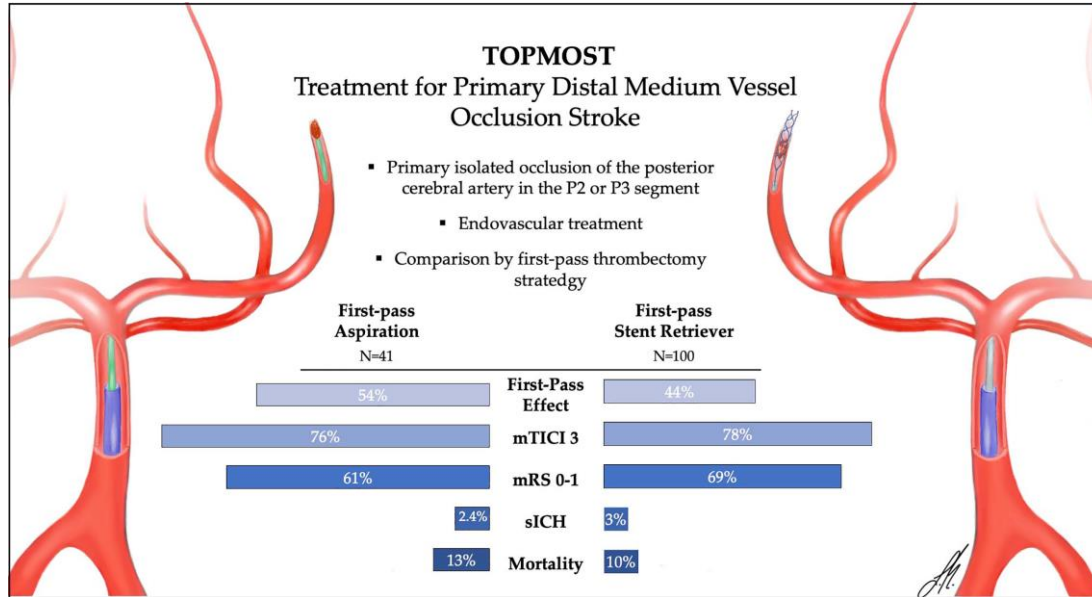
No clinical benefit (outcome)

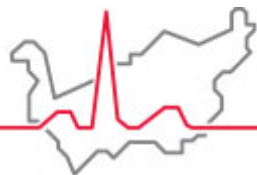
↑sICH



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Is the **outcome device dependant**? Aspiration vs Stent Retriever





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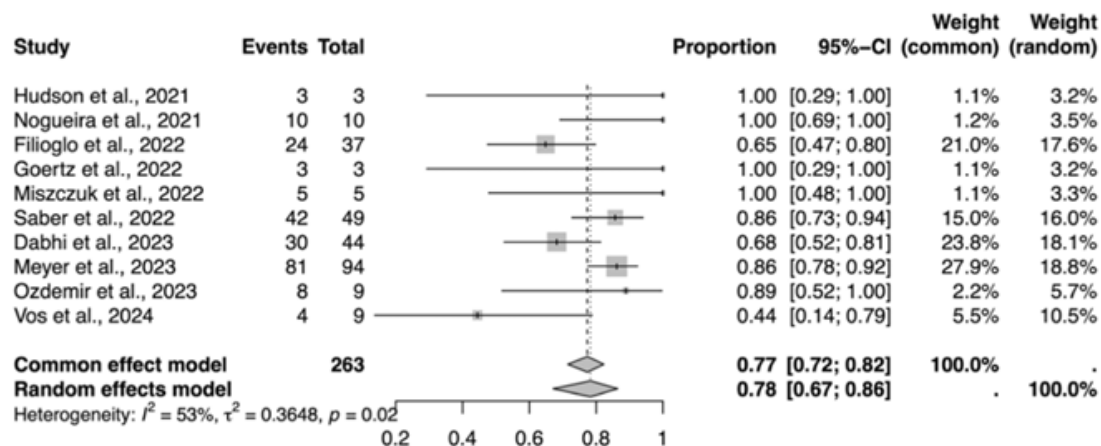
EVT in ACA occlusion ? Meta-analysis

ACA Occlusion Site (n=159)		
A1		29 (18.2)
A2		89 (56)
A3		38 (23.9)
A4		3 (1.9)
Procedural tPA/TNK Given (n=264)		
Yes		110 (41.7)
EVT Technique (n=64)		
Solumbra		25 (39.1)
ADAPT		22 (34.4)
Stent retriever		20 (31.3)

This meta-analysis provides the largest pooled analysis of acute ischemic primary ACA occlusions, encompassing 265 patients across 10 studies. Our meta-analysis found that mTICI $\geq 2b$ rates were comparable to those in LVO and other MeVO cohorts, with an overall mTICI $\geq 2b$ rate of 78 % and a low complication rate of 4 %. However, there were lower rates of favorable 3-month mRS scores and higher mortality rates, reflecting the increased morbidity and mortality associated with ACA occlusions. These findings emphasize the need for further investigation with multicenter clinical trials to understand the precise role of EVT in this unique patient population.

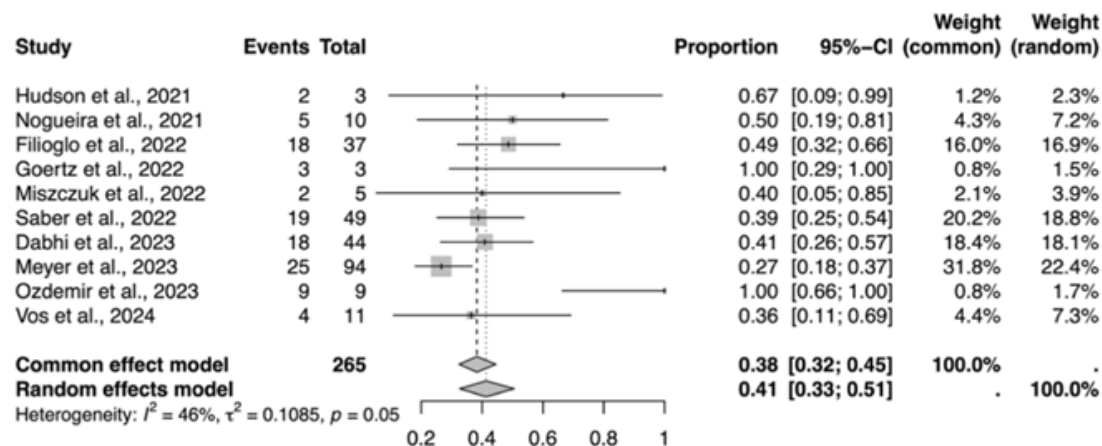
A

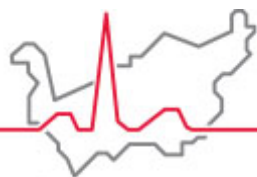
mTICI scores 2b-3



B

mRS 0-2





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ACA EVT (TOPMOST registry)

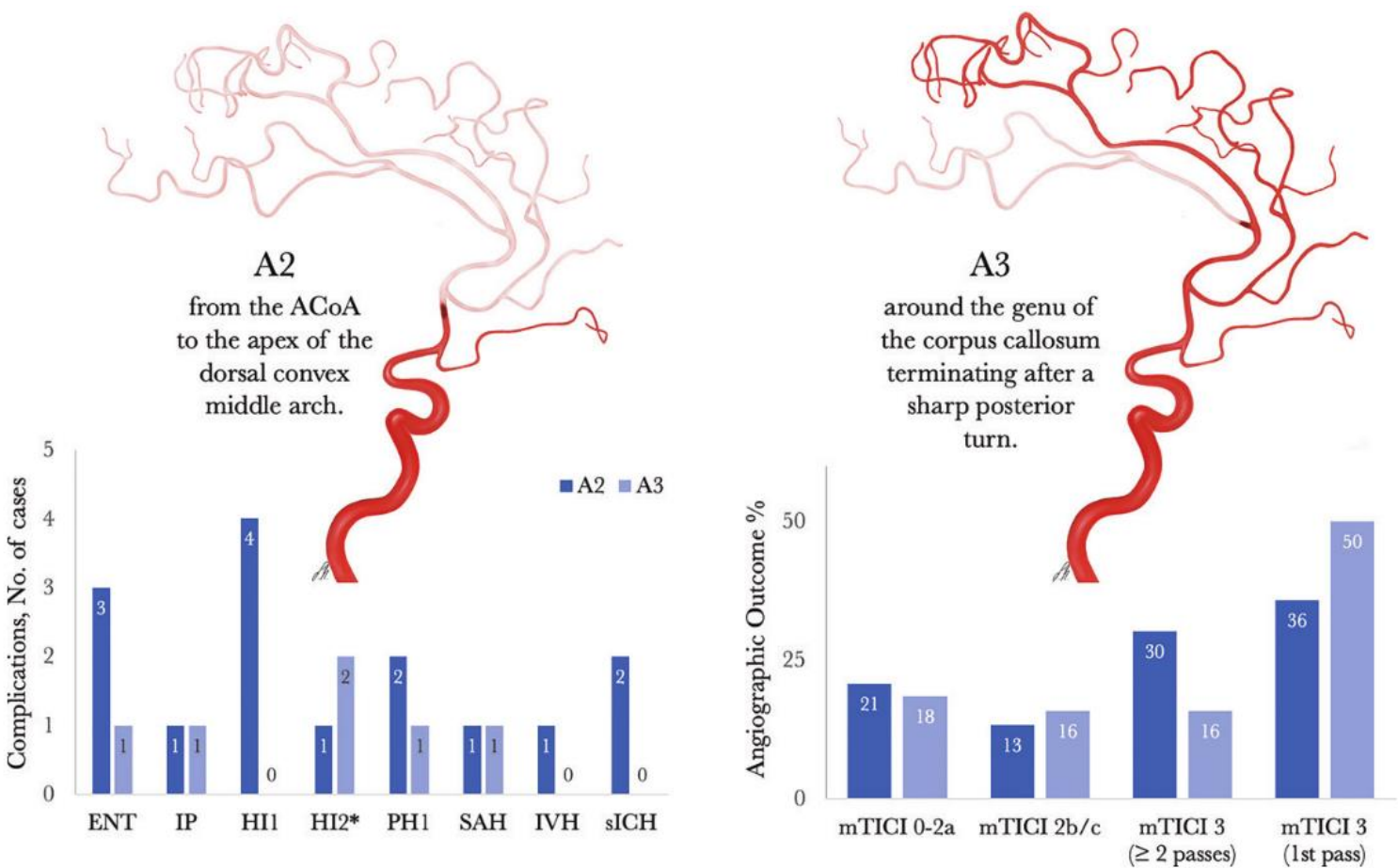


Figure 4: Procedural endovascular complications and angiographic outcome stratified by occluded vessel segments. * Includes one case with an A4 occlusion. ACoA = anterior communicating artery, ENT = emboli to new territory, HI = hemorrhagic transformation, IP = itrogenic perforation, IVH = intraventricular hemorrhage, mTICI = modified thrombolysis in cerebral infarction, PH = parenchymal hemorrhage, SAH = subarachnoid hemorrhage, sICH = symptomatic intracerebral hemorrhage.

Table 4: Multivariable Logistic Regression Analysis for Favorable Functional Outcome in Patients after Propensity Score Matching

Parameter	Adjusted OR	P Value
Treatment (MT)	1.57 (0.43, 5.70)	.49
Sex (male)	1.08 (0.29, 4.04)	.90
Age (increasing)	0.93 (0.89, 0.98)	.006*
Prestroke mRS (increasing)	0.42 (0.20, 0.88)	.02*
NIHSS admission (increasing)	0.79 (0.68, 0.91)	.001*
Occluded segment (distal)	1.93 (0.58, 6.39)	.28
IVT (yes)	1.67 (0.43, 6.43)	.45

Note.—The model sample size was 75 patients. Parenthetical statements are the reference selected in the model. Data in parentheses are 95% CIs. Favorable functional outcome was indicated by a modified Rankin scale (mRS) score of 0–2. Data were collected at 90-day follow-up in all patients after propensity score matching. IVT = intravenous thrombolysis; OR = odds ratio, mRS = modified Rankin scale, MT = mechanical thrombectomy, NIHSS = National Institutes of Health Stroke Scale.

* Distal was an indicator for A3/A4 occlusions in reference to A2 occlusions.



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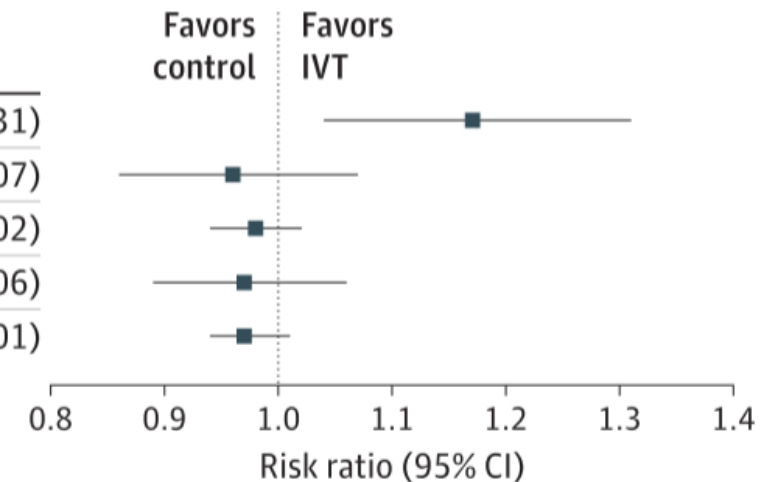
IVT / EVT in low NIHSS <6

Thrombolysis With Tenecteplase for Minor Disabling Stroke

Secondary Analysis of the TEMPO-2 Randomized Clinical Trial

Figure 2. Summary of Studies Evaluating Intravenous Thrombolysis (IVT) in Minor Ischemic Stroke

Source	Thrombolytic	Control	Patients with disabling deficits, %	Sample size, No.	Risk ratio (95% CI)
Pooled analysis (2014) ³	Alteplase	Placebo ^a	Except for IST-3 ^a	666 ^a	1.17 (1.04-1.31)
PRISMS (2018) ⁴	Alteplase	Aspirin	0 ^b	313	0.96 (0.86-1.07)
ARAMIS (2023) ⁵	Alteplase	DAPT (77%) ^c	0 ^d	719	0.98 (0.94-1.02)
TEMPO-2 (2024) ¹⁰	Tenecteplase	DAPT (58%)	11 ^e	884	0.97 (0.89-1.06)
PUMICE (2025) ¹⁸	Prourokinase	DAPT (91%)	11 ^e	1446	0.97 (0.94-1.01)



➔ **Safety issue: ↑sICH and stroke progression**

➔ **Is mRS a good surrogate marker of treatment efficacy?**

➔ **Clinical presentation of cortical vascular territories is highly variable**

➔ **DAPT seems to win the mRS contest**

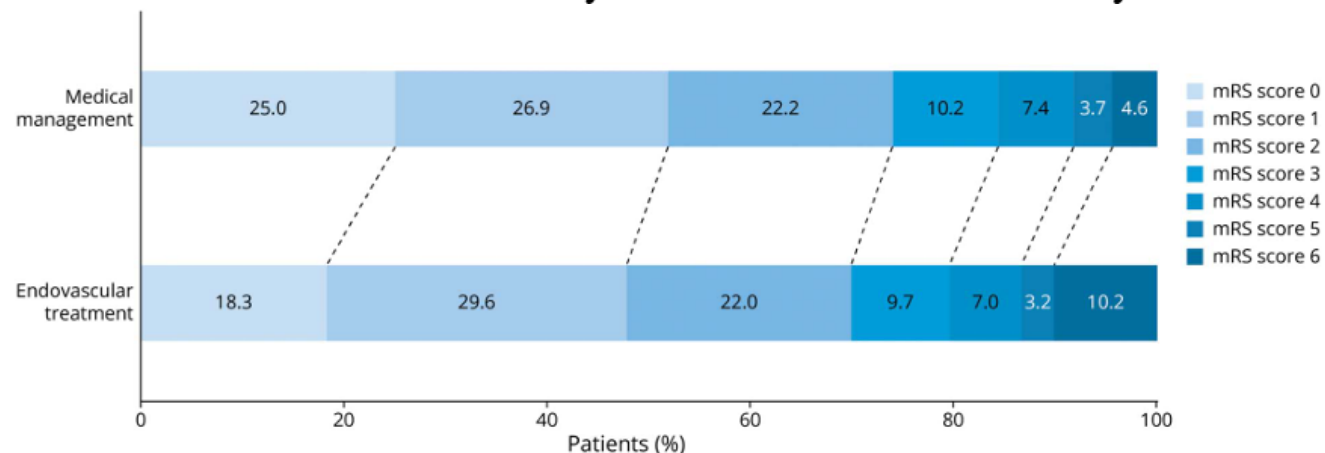
Endovascular Therapy for NIHSS ≤ 5

How Low Should We Go?

Susanne G.H. Olthuis¹ and Wim H. Van Zwam²

Endovascular Therapy for Patients With Low NIHSS Scores and Large Vessel Occlusion in the 6- to 24-Hour Window

Analysis of the CLEAR Study



➔ **EVT does not improve clinical outcome vs MM**



JAMA Neurology | Original Investigation

Medical Management vs Mechanical Thrombectomy for Mild Strokes

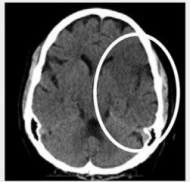
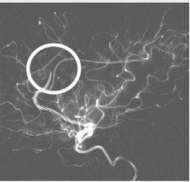
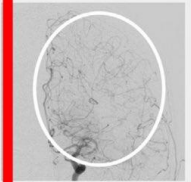
An International Multicenter Study and Systematic Review and Meta-analysis

Nitin Goyal, MD; Georgios Tsivgoulis, MD; Konark Malhotra, MD; Muhammad F. Ishfaq, MD; Abhi Pandhi, MD; Michael T. Frohler, MD; Alejandro M. Spiotta, MD; Mohammad Anadani, MD; Marios Psychogios, MD; Volker Maus, MD; Adnan Siddiqui, MD; Muhammad Waqas, MD; Peter D. Schellinger, MD; Marcel Groen, MD; Christos Krogias, MD; Daniel Richter, MD; Maher Saqqur, MD; Pablo Garcia-Bermejo, MD; Maxim Mokin, MD; Ronen Leker, MD; Jose E. Cohen, MD; Aristeidis H. Katsanos, MD; Georgios Magoufis, MD; Klearchos Psychogios, MD; Vasileios Lioutas, MD; Meg VanNostrand, MD; Vijay K. Sharma, MD; Maurizio Paciaroni, MD; Alexandros Rentzos, MD; Hazem Shoirah, MD; J. Mocco, MD; Christopher Nicklele, MD; Violiza Inoa, MD; Daniel Hoit, MD, MPH; Lucas Eljovich, MD; Andrei V. Alexandrov, MD; Adam S. Arthur, MD, MPH

 Supplemental content

IMPORTANCE The benefit of mechanical thrombectomy (MT) in patients with stroke presenting with mild deficits (National Institutes of Health Stroke Scale [NIHSS] score <6) owing to emergency large-vessel occlusion (ELVO) remains uncertain.

OBJECTIVE To assess the outcomes of patients with mild-deficits ELVO (mELVO) treated with MT vs best medical management (bMM).

	Anterior circulation LVO	Basilar artery occlusions	Low ASPECT score	Distal occlusions	Low NIHSS score
Image representation					
Current evidence	 No EVT EVT	 No EVT EVT	 No EVT EVT	 No EVT EVT	 No EVT EVT
Expected evidence (until 2024)	None	Potentially 2 RCTs	Up to 6 RCTs	2-3 RCTs	2 RCTs



Endovascular Therapy for Low NIHSS Ischemic Strokes

Lowering The Bar For EVT Selection

Principal Investigators:

- Andrew Demchuk, MD
- Pooja Khatri, MD, Msc
- Simon Nagel, MD
- Raul Nogueira, MD

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Welcome

ENDOW is a Phase 2/3, prospective, randomized, open-label, blinded-endpoint (PROBE) adaptive two-stage design trial allowing for early stopping for efficacy or futility after the first stage or continuation with stage two including the option of recalculating the sample size. This study will be testing efficacy and safety of immediate mechanical thrombectomy (iMT) initiated within 8 hours in conjunction with medical management versus initial medical management (iMM) alone administered in patients presenting with cerebral ischemia in the setting of proximal large vessel occlusions (LVO) and low baseline NIHSS scores (NIHSS 0-5). LVO is defined as occlusion involving the internal carotid artery (ICA), the M1 and/or M2 segments of the middle cerebral artery (MCA). The primary endpoint will be a categorical shift across all levels on the modified Rankin Scale (mRS) at 90-days post-randomization. The hypothesis is that iMT will lead to an improved clinical outcome at 90 days. Interim analysis will be performed after the primary endpoint is available for a total of 175 randomized patients.

Data Required for Randomization

• Consent Obtained	Yes or No
• Thrombolytic Given (tPA/TNK)	Yes or No
• Occlusion Site	ICA or M1/M2
• Age	<70 years or ≥70 years
• NIHSS	0-2 or 3-5



Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOW) NCT04167527

Raul Gomes Nogueira, Emory University

IN EXTREMIS
MOSTE] [LASTE

Minor Stroke Therapy Evaluation (MOSTE) NCT03796468

Vincent COSTALAT, PU-PH

Caroline ARQUIZAN, PH

Bertrand LAPERGUE, PH

Tudor JOVIN, PU-PH

Hôpital Gui de Chauiac

Hôpital Gui de Chauiac

Hôpital Foch

Cooper Neurological Institute

MOSTE]

240 inclusions

Estimated Enrollment :

824 patients

Interim analysis:

274 et 548 patients

<https://www.endow.org>

<https://www.inextremis-study.com/>

https://twitter.com/XiaochuanHuo/status/1527695190554685441?s=20&t=rjfUwQR4_BdqXr0R4Qntvg

Very late EVT > 24h

Endovascular treatment for acute ischemic stroke beyond the 24-h time window: Selection by target mismatch profile

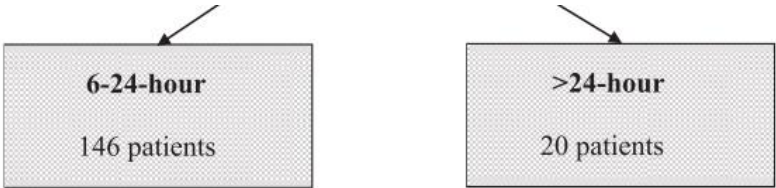


Table 4. The outcomes between two groups after propensity score matching.

	All (n = 49)	Symptom onset >24 h (n = 18)	Symptom onset 6–24 h (n = 31)	p
mRS 0–2 at 90 days (%)	26 (53.1)	9 (50.0)	17 (54.8)	0.74
mRS ordinal shift	2.0 (2.0–4.0)	2.5 (2.0–4.0)	2.0 (1.0–3.5)	0.41
TICI 2b-3 (%)	43 (87.8)	16 (88.9)	27 (87.1)	1.00
Symptomatic ICH (%)	2 (4.08)	0 (0)	2 (6.45)	0.53
Any hemorrhage (%)	10 (20.4)	0 (0)	10 (32.3)	0.008
Mortality (%)	6 (12.2)	3 (16.7)	3 (9.68)	0.50

mRS: modified Rankin Scale; TICI: thrombolysis in cerebral infarction; ICH: intracerebral hemorrhage.

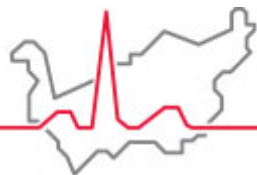
Conclusion

Our study conducted in a developing country suggests that EVT may be performed safely and effectively in LVO patients beyond 24 h from symptom onset selecting by target mismatch profile.



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IA thrombolysis after EVT



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Post-EVT IA thrombolysis trials

Trial	CHOICE	POST-TNK	POST-UK	ATTENTON-IA	ANGEL-TNK	DATE	PEARL
Year	2022	2025	2025	2025	2025	2025	2025
Country	Spain	China	China	China	China	China	China
Occlusion site	ICA, M1, M2 or PCA	ICA, M1, or M2	ICA, M1, or M2	Basilar, vertebral, or P1	ICA, M1, or M2	ICA, M1, or M2	ICA, M1, or M2
Thrombolytic agent	Alteplase (0.225 mg/kg)	Tenecteplase (0.0625 mg/kg)	Urokinase (100 000 IU)	Tenecteplase (0.0625 mg/kg)	Tenecteplase (0.125 mg/kg)	Tenecteplase (0.0625/0.03125 mg/kg)	Alteplase (0.225 mg/kg)
Participations EVT + IAT vs EVT (n)	62 vs 52	269 vs 271	267 vs 267	104 vs 104	126 vs 129	92 vs 65	164 vs 160
Time from onset to randomisation	24 hours	24 hours	24 hours	24 hours	4.5–24 hours	24 hours	24 hours
eTICI score	2b50-3	2c-3	2c-3	2b50-3	2b50-3	2b50-3	2b50-3
IVT before EVT	With or without	Without	Without	With or without	Without	Without	With or without

EVT = endovascular thrombectomy; eTICI = extended thrombolysis in cerebral infarction; IAT = intra-arterial thrombolysis; ICA = internal carotid artery; IU = international units; IVT = intravenous thrombolysis; M1 = main trunk of the middle cerebral artery; M2 = first-order branch of the main trunk of the middle cerebral artery; PCA = posterior cerebral artery; P1 = first segment of the posterior cerebral artery.

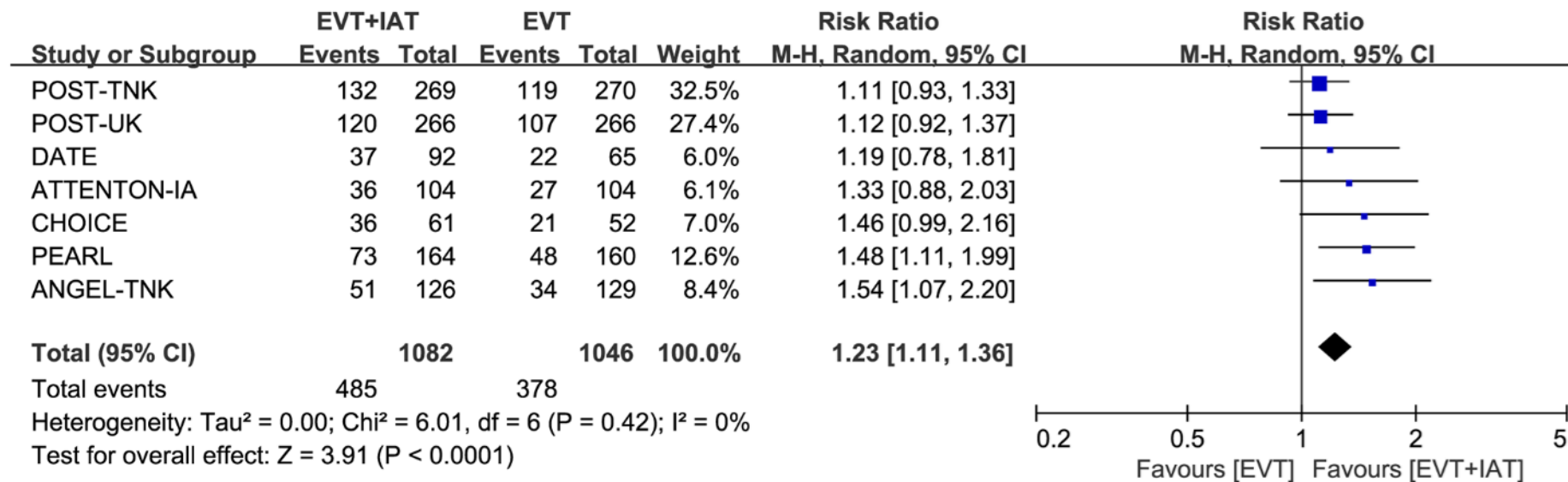
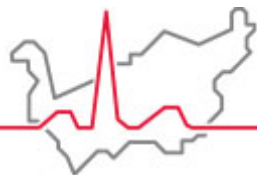
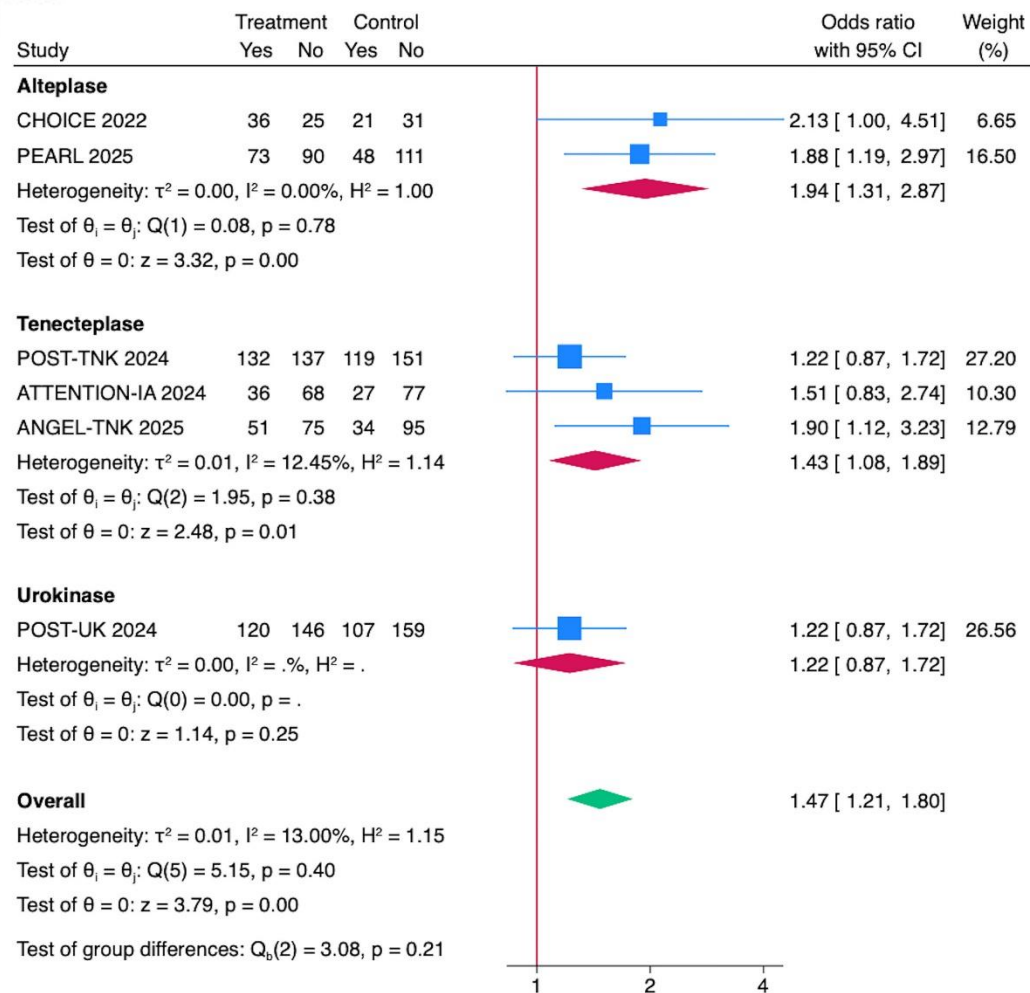


Figure 2. Forest plots for the modified Rankin Scale Score of 0–1 at 90 days.

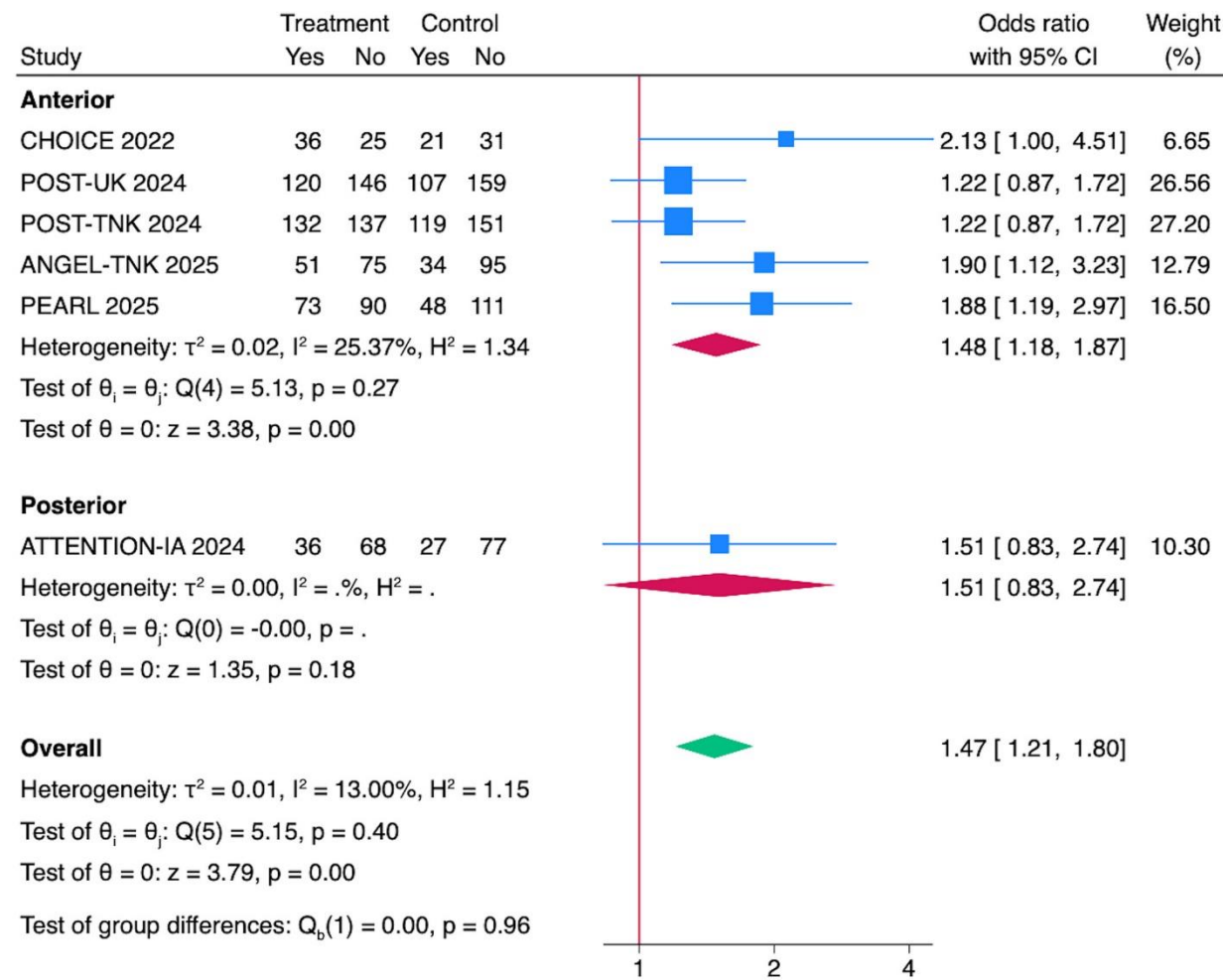


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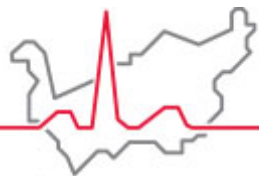
Results (3m mRS 0-1) according to thrombolytics and circulation



Random-effects REML model



Random-effects REML model



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tPA or TNK? → tPA ranked better!

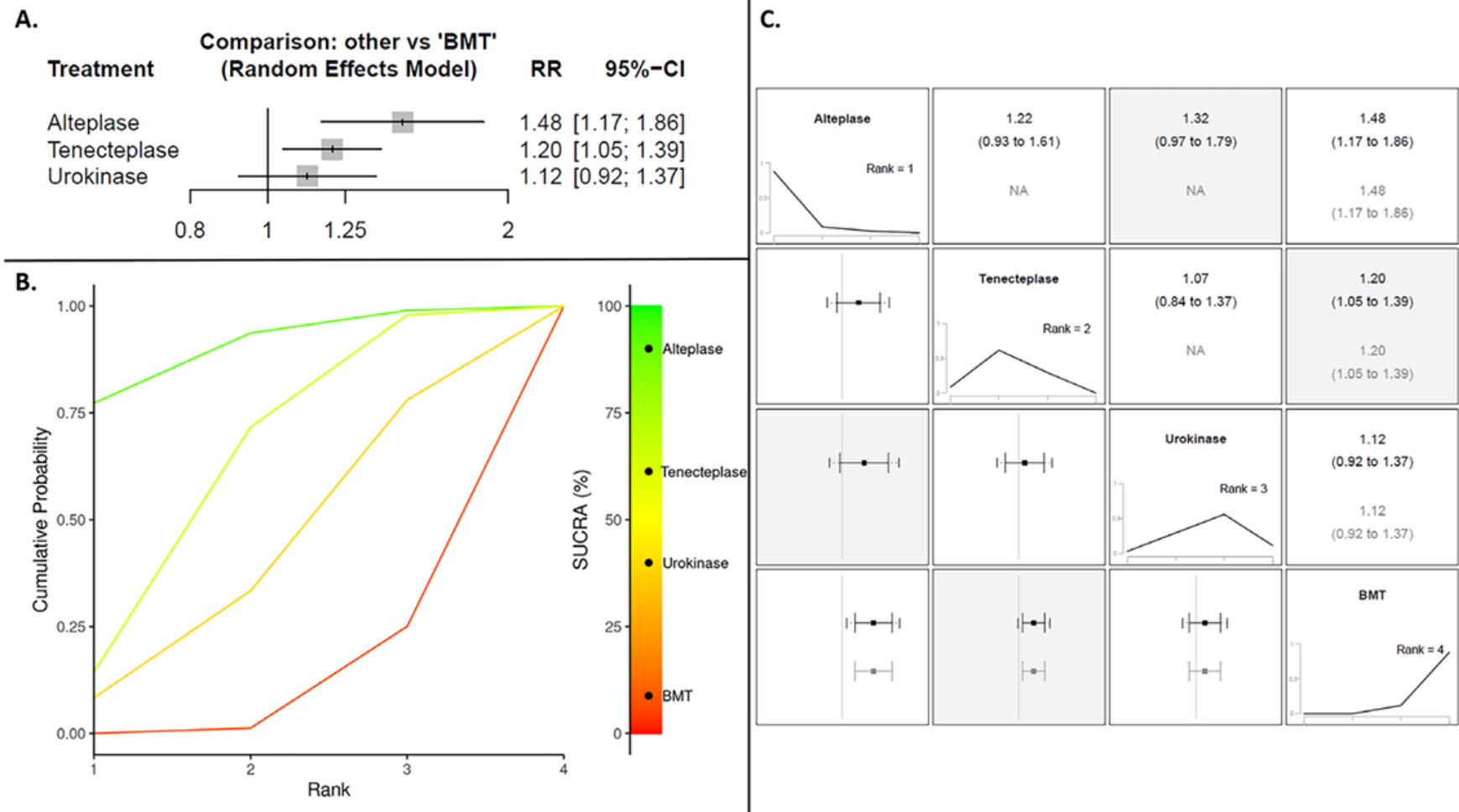


FIGURE 3 | Forest plot of the random-effects network meta-analysis (NMA) presenting the risk ratio of excellent functional outcome at 3 months according to the treatment group, using best medical treatment (BMT) as reference (Panel A). SUCRA plot for the excellent functional outcome at 3 months with higher Surface Under the Cumulative Ranking Curve (SUCRA) values and cumulative ranking curves nearer the top left indicating better performance (Panel B). Summary forest plot for the risk ratio of excellent functional outcome at 3 months: NMA results in black; pairwise meta-analysis results in gray; 95% confidence interval presented as error bars; interventions are ranked and sorted by SUCRA value.



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IA thrombolysis after EVT

Study	Sample size	Population (Anterior Circulation LVO)				Intervention		Results	
		TICI 2b50	IVT	Time window	Baseline NHISS (median)	IA Dose	IA Drug	90-day mRS 0-1 RR/RD [95%CI]	sICH
PEARL	324	+	+	0-24h	15	25%	Alteplase 0.225 mg/kg	44.8% vs 30.2% 1.45 [1.08-1.96] P = 0.01	4.3% vs 5% P = 0.67
ANGEL-TNK	256	+	-	4.5-24h	15/16	50%	Tenecteplase 0.125 mg/kg	40.5% vs 26.4% 1.44 [1.06-1.95] P=0.02	5.6% vs 6.2% P=0.92
CHOICE*	121	+	+	0-24h	14	25%	Alteplase 0.225 mg/kg	59.0% vs 40.4% 18.4% [0.3-36.4] P = 0.047	0% vs 3.8%
POST-TNK	540	-	-	0-24h	15	25%	Tenecteplase 0.0625 mg/kg	49.1% vs 44.1% 1.15 [0.97-1.36] P = 0.11	6.3% vs 4.4% P = 0.35
POST-UK	535	-	-	0-24h	15	~7-10%	Urokinase 100,000IU	45.1% vs 40.2% 1.13 [0.94-1.36] P = 0.19	4.1% vs 4.1% P = 0.91

CLINICAL PERSPECTIVE

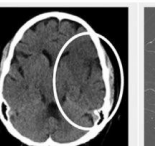
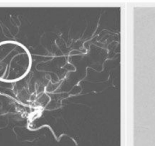
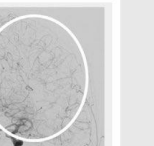
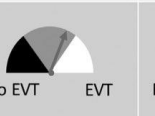
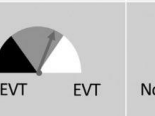
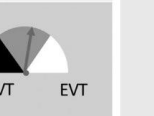
- This study indicated that intra-arterial thrombolysis following successful endovascular thrombectomy in patients with stroke is safe without increasing the risk of symptomatic intracranial hemorrhage and 90-day mortality.
- Intra-arterial thrombolysis following successful endovascular thrombectomy significantly improved the rate of disability-free survival at 90 days, particularly in patients without complete recanalization (expanded Thrombolysis in Cerebral Infarction 2b50/67) and those without prior intravenous thrombolysis.
- The therapeutic effect of intra-arterial thrombolysis may be further improved if patient selection in future studies is refined by identifying with microcirculation dysfunction after successful endovascular thrombectomy. This might be achieved using digital subtraction angiography “perfusion” and flat-panel computed tomography perfusion.



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BA, VA, PCA

Posterior circulation EVT

	Anterior circulation LVO	Basilar artery occlusions	Low ASPECT score	Distal occlusions	Low NIHSS score
Image representation					
Current evidence	 No EVT → EVT	 No EVT → EVT	 No EVT → EVT	 No EVT → EVT	 No EVT → EVT
Expected evidence (until 2024)	None	Potentially 2 RCTs	Up to 6 RCTs	2-3 RCTs	2 RCTs

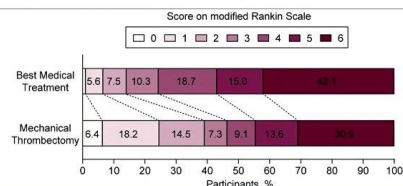


BAOCHE

NCT02737189

0217 Basilar Artery Occlusion Chinese Endovascular Trial (BAOCHE)

Primary analysis (N=217, ITT population)



	Thrombectomy (N=110)	BMT (N=107)	Unadjusted OR (95% CI), P Value	Adjusted OR (95% CI)*, P Value
mRS 0-3 at 90 days, n (%)	51 (46.4)	26 (24.3)	2.69 (1.51, 4.81) P=0.001	2.92 (1.56, 5.47) P=0.001

*Odds ratio was adjusted for minimization factor: age (≤ 70 or >70 years), baseline NIHSS (6-20 or >20), therapeutic window (6-12h or $>12h$).

ESOC 2022

The Voice of Stroke in Europe

eso-conference.org



Tudor Jovin

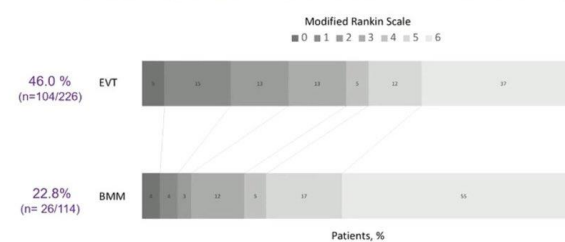


ATTENTION

NCT04751708

ENDOVASCULAR TREATMENT FOR ACUTE BASILAR ARTERY OCCLUSION - A MULTICENTER RANDOMIZED CONTROLLED TRIAL (ATTENTION)

Primary Outcome: mRS 0-3 at 90 days



Measure of Effect	Adjusted Value(95% CI)	P value
Risk Ratio	2.1 (1.5, 3.0)	<0.001
Risk Difference	24.2% (15.0%, 33.5%)	<0.001

NNT=4

Adjusted for age, baseline NIHSS, pre-morbid mRS, time from onset to randomization. The 95% CI not adjusted for multiple comparisons.

ATTENTION

ESOC 2022

European Stroke Organisation Conference 2022

4-8 May 2022, Lyon, France



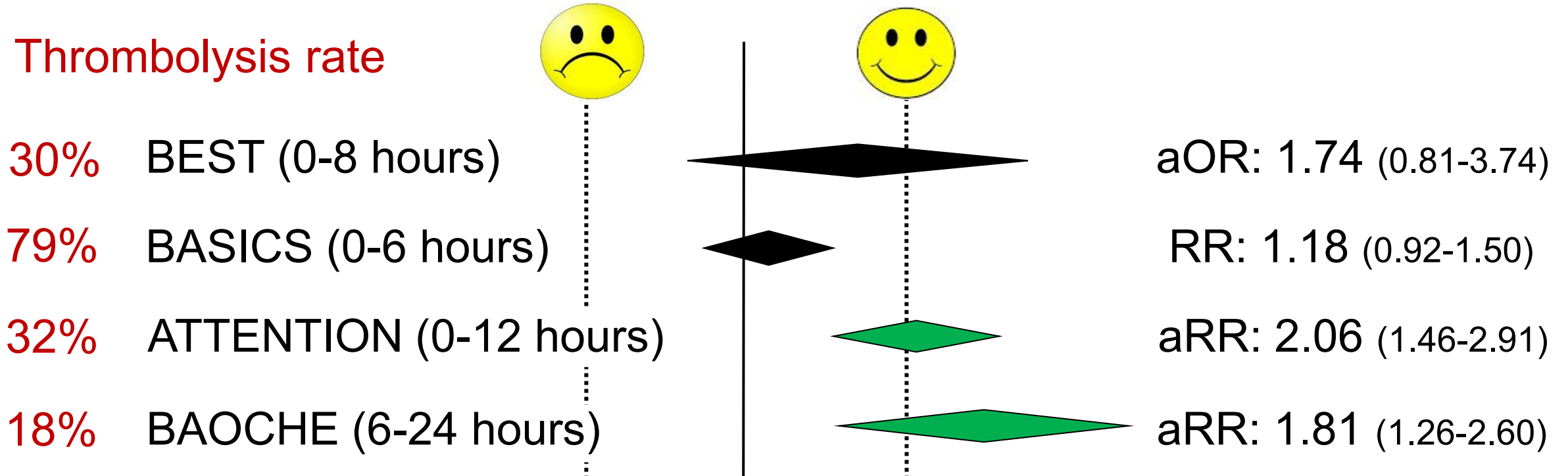
Raul Nogueira

ESOC 2022

ESOC 2022

Does thrombectomy work (vs. «BMT») in basilar artery occlusion ?

Thrombolysis rate



→ EVT seems to work in Asian patients with moderate-to-severe deficits, limited early ischemic changes, and limited thrombolysis rates

BEST: Liu & Nogueira, Lancet Neurol 2020; BASICS: Langezaal & van der Hoeven, NEJM 2021

décembre 2025

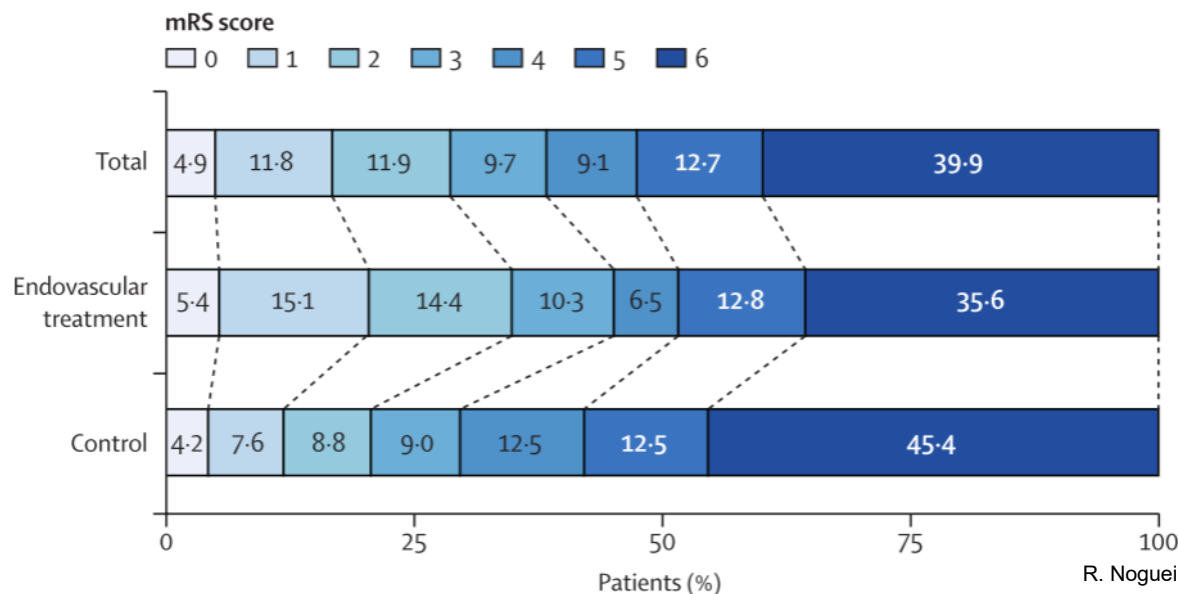
ATTENTION: Tao NEJM 2022; BAOCHE: Jovin NEJM 2022

Table 3 Key characteristics

	BASICS	BEST	ATTENTION	BAOCHE
Date	2011–2019	2015–2017	2021–2022	2016–2022
Symptom onset to inclusion (hours)	0–6	0–8	0–12	6–24
Number screened	424	288	507	Data not available
Number of participants	300	131	340	217
Crossover (percentage)	3/154 (1.9) to BMT 7/146 (4.7) to MT	3/66 (4.5) to BMT 14/65 (21.5) to MT	3/226 (1.3) to BMT 3/114 (2.6) to MT	1/110 (0.9) to BMT 4/107 (3.7) to MT
Median NIHSS at presentation (IQR)	Intervention: 21.9 Control: 22.1 (IQR not available)	Intervention: 32 (18–38) Control: 26 (13–37)	Intervention: 24 (15–35) Control: 24 (14–35)	Intervention: 20 (14.5–29) Control: 19 (12–30)
Intravenous thrombolysis (%)	Intervention: 121/154 (78.6) Control: 116/146 (79.5)	Intervention: 18/66 (27) Control: 21/65 (32)	Intervention: 69/226 (30.5) Control: 39/114 (34.2)	Intervention: 15/110 (13.6) Control: 23/107 (21.5)
Blinding	Open-label, blinded outcome assessment	Open-label, blinded outcome assessment	Open-label, blinded outcome assessment	Open-label, blinded outcome assessment
mRS (≤ 3) (percentage)	Intervention: 68/154 (44.1) Control: 55/146 (37.6)	Intervention: 28/66 (42.4) Control: 21/65 (32.3)	Intervention: 104/226 (46) Control: 26/114 (22.8)	Intervention: 51/110 (46.3) Control: 26/107 (24.2)
Mortality at day 90 (percentage)	Intervention: 59 (38.3) Control: 63 (43.2)	Intervention: 22 (33.3) Control: 25 (38.4)	Intervention: 83 (36.7) Control: 63 (55.2)	Intervention: 34 (30.9) Control: 45 (42.1)
sICH (percentage)	Intervention: 6 (4.5) Control: 1 (0.7)	Intervention: 5 (8) Control: 0	Intervention: 12 (5) Control: 0	Intervention: 6 (8.8) Control: 1 (2.3)
Follow up:	24 hrs, 90 days	24 hrs, 90 days	24 hrs, 90 days	24 hrs, 90 days, 6 months, 1 year

Endovascular therapy for acute vertebrobasilar occlusion (VERITAS): a systematic review and individual patient data meta-analysis

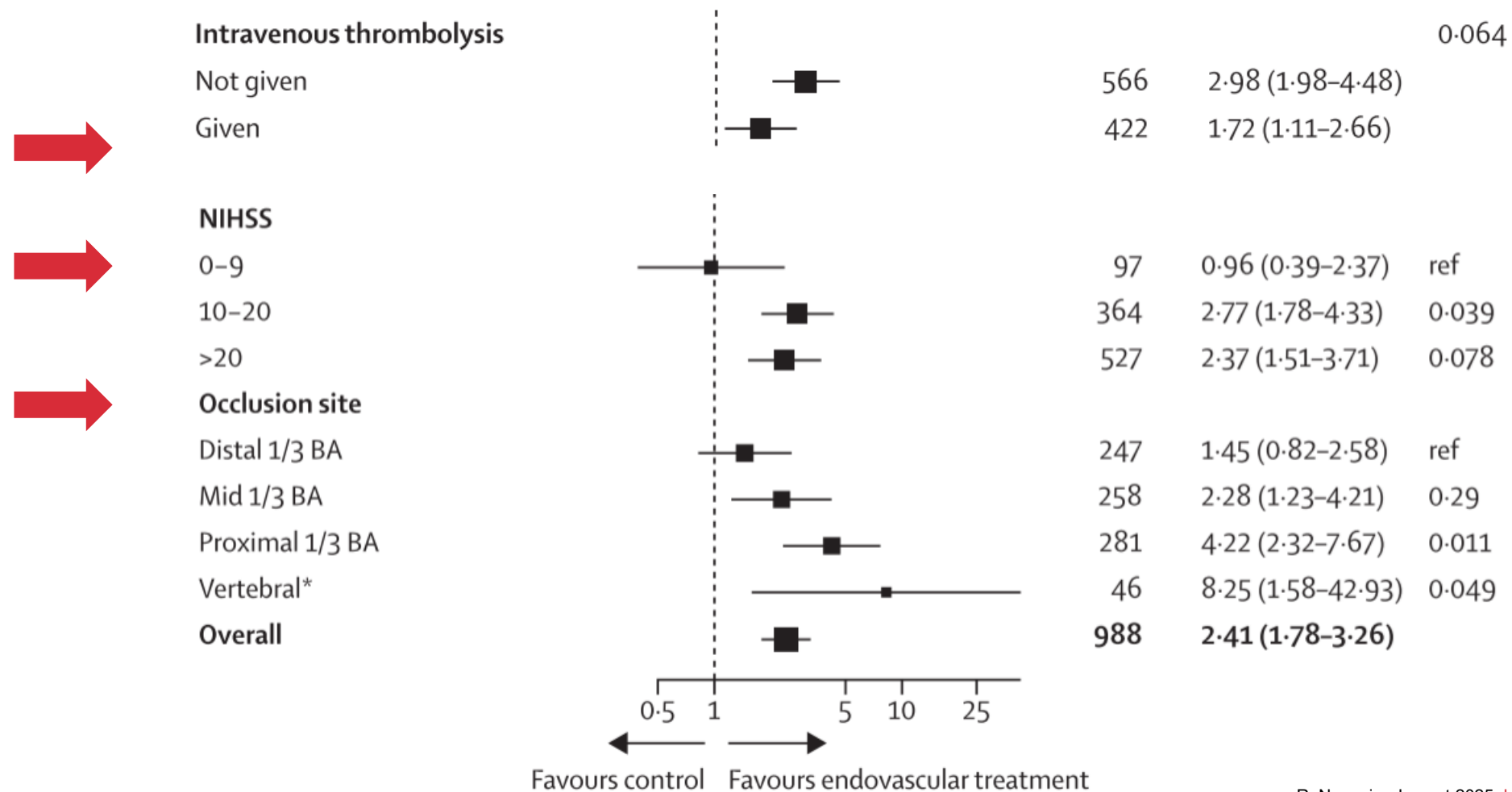
Occlusion Site*	Control	EVT	Total
Distal 1/3 BA	110/356 (31%)	137/477 (29%)	247/833 (30%)
Mid 1/3 BA	107/356 (30%)	151/477 (32%)	258/833 (31%)
None	0/356	1/477 (<1%)	1/833 (<1%)
Proximal 1/3 BA	125/356 (35%)	156/477 (33%)	281/833 (34%)
Vertebral	14/356 (4%)	32/477 (7%)	46/833 (6%)





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VERITAS: Subgroup analysis



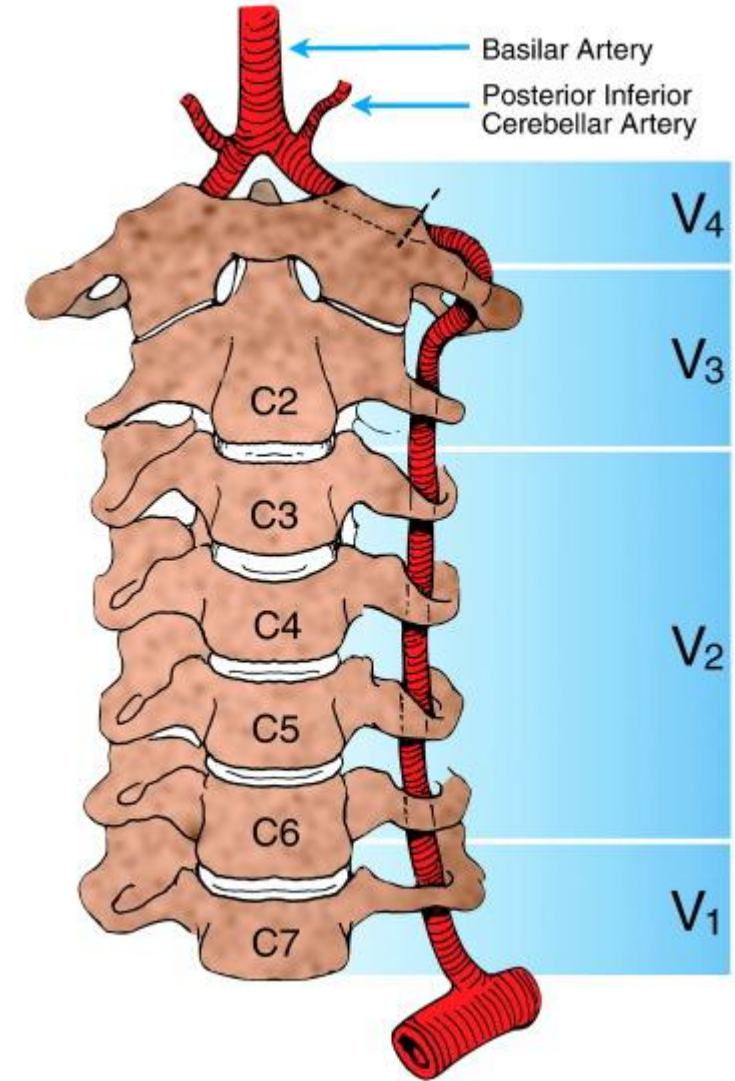


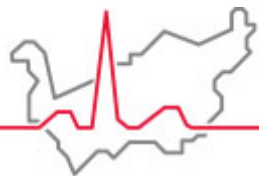
Acute **isolated vertebral artery stroke** ... EVT or NOT ?

BEST REVASCULARISATION APPROACH FOR POSTERIOR CIRCULATION STROKES WITH ISOLATED VERTEBRAL ARTERY OCCLUSION: DESIGN OF THE “BRAVO” STUDY

A. Salerno¹, D. Strambo¹, G. Marie², G. Costamagna¹,
V. Dunet², G. Saliou², P. Michel¹

The international, multicenter retrospective BRAVO study [29^{***}] is the most comprehensive analysis on iVAO revascularization to date. This study included people treated conservatively, with IVT, and with EVT. The findings suggest that **IVT is a well tolerated and possibly effective treatment option for iVAO** patients, showing a higher probability of arterial recanalization compared to conservatively treated patients. Conversely, patients who underwent **EVT had significantly worse functional outcome compared to those receiving best medical treatment**. This observation seems to be at least in part explained by **higher syICH rates** [odds ratio (OR) 3.74, CI 1.13–12.43] and to **more frequent early neurological deterioration** of ischemic origin (ENDi) (OR 7.29, CI 4.07–13.07).

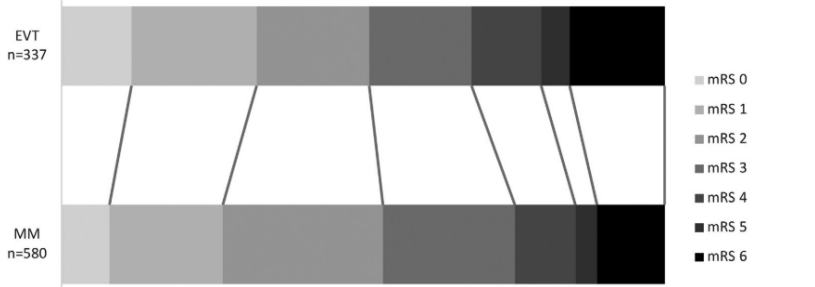




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Acute isolated PCA stroke ... EVT or NOT ?

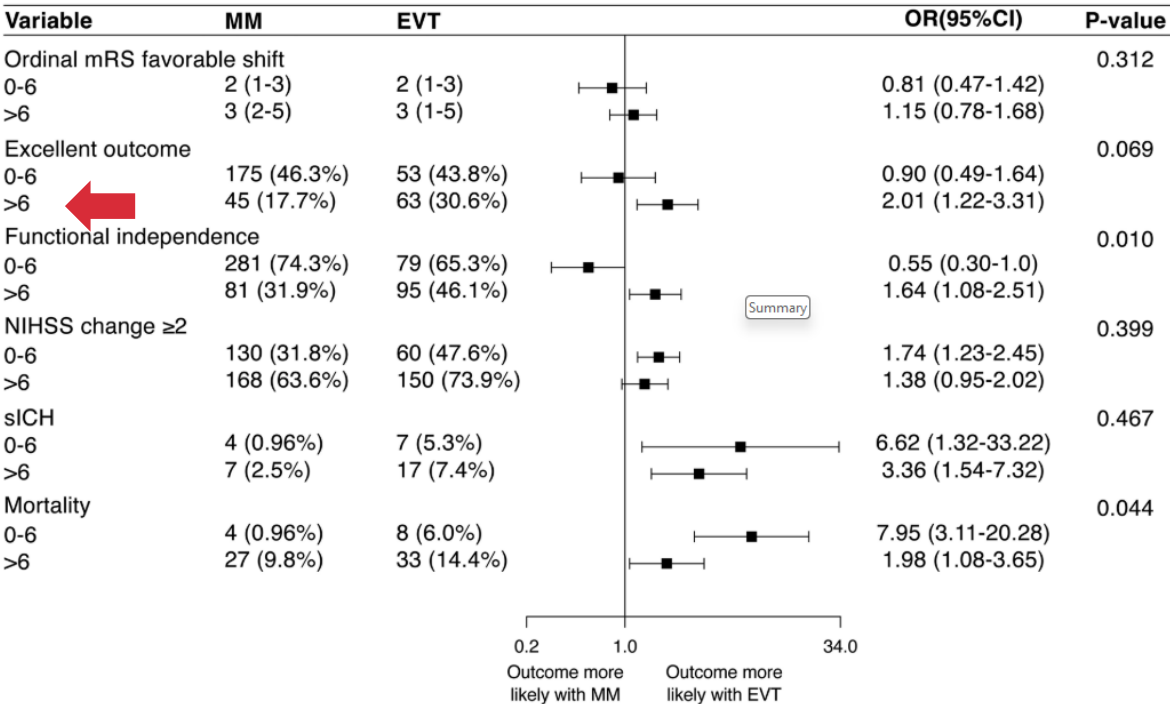
PLATO Study
substudy



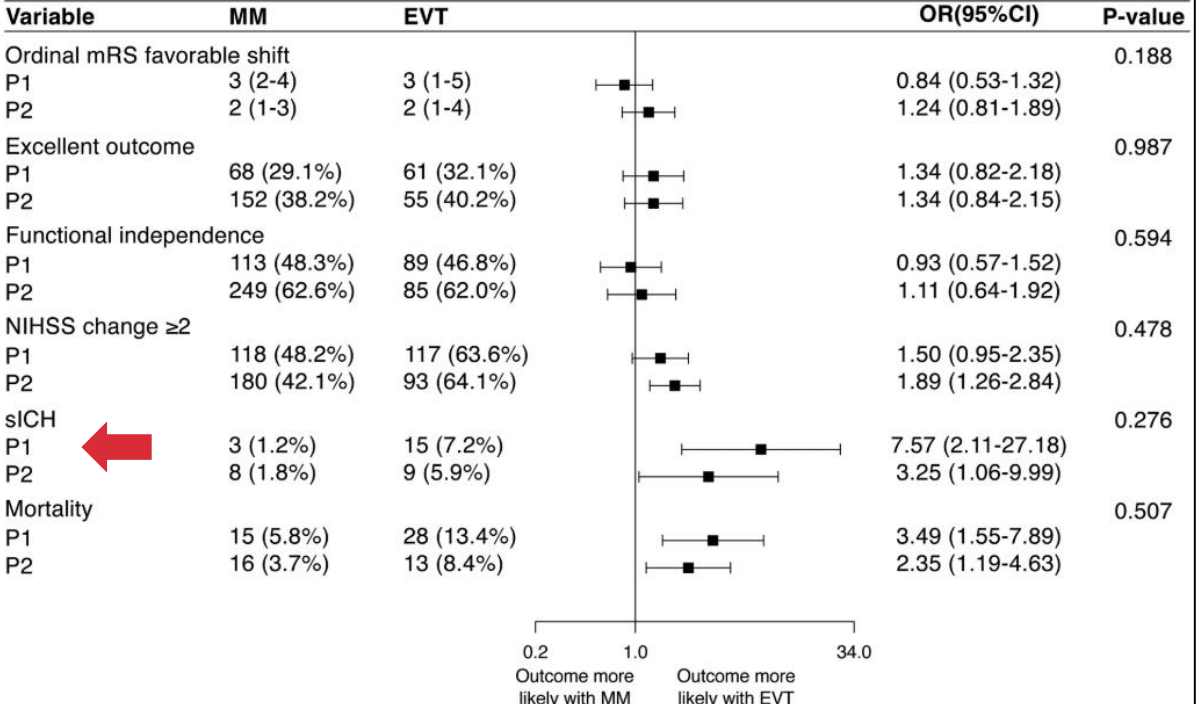
Excellent outcome (mRS score 0–1, 90 d; n=917)				
MM	580	155 (26.7)	Referent	
EVT	337	109 (32.3)	1.31 (0.98–1.76)	0.070

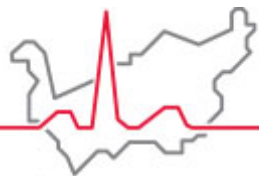
sICH (n=1018)*				
MM	644	11 (1.7)	Referent	
EVT	374	23 (6.2)	3.77 (1.82–7.83)	0.0004

A



B





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Outcome depending on NIHSS

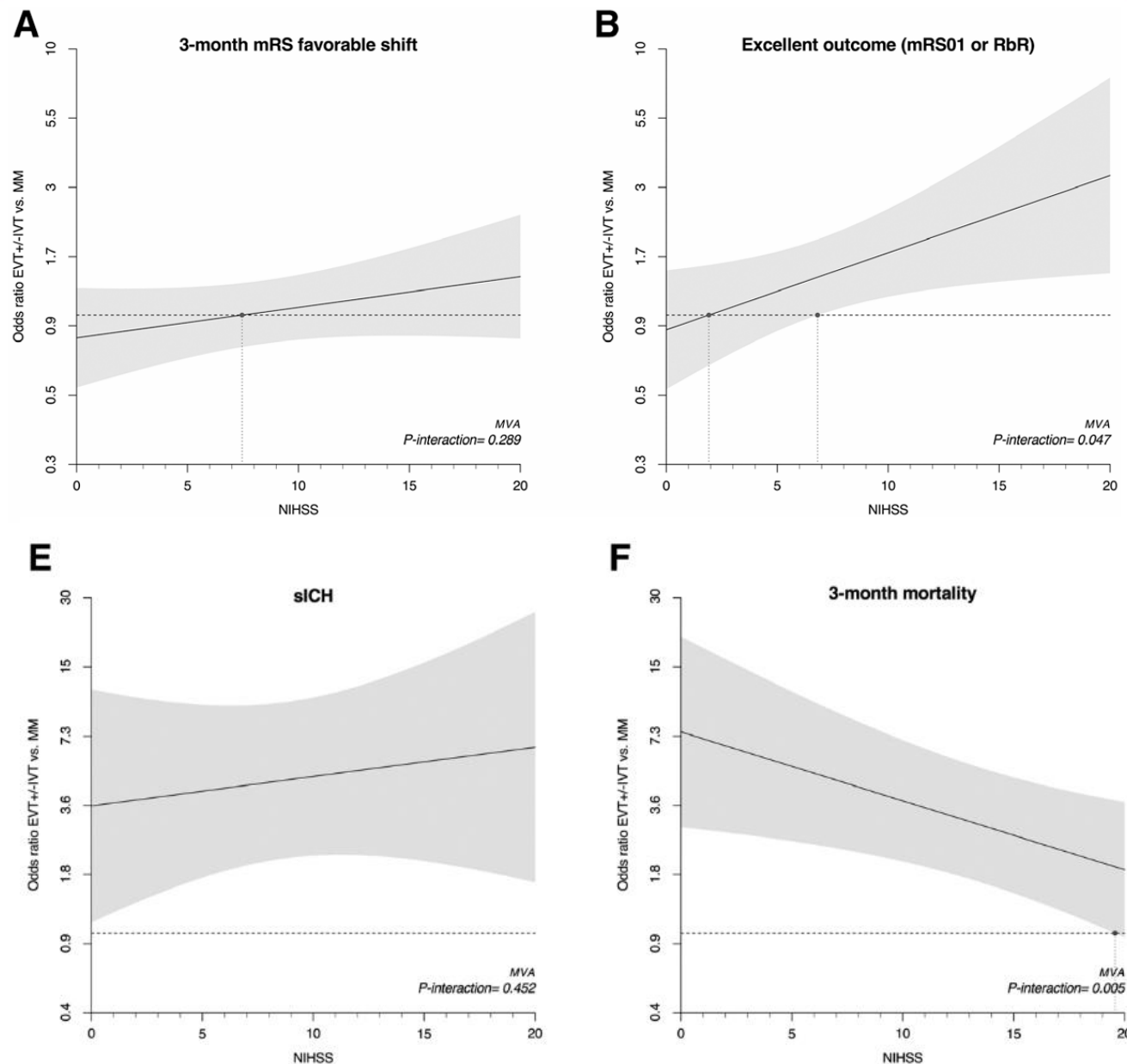


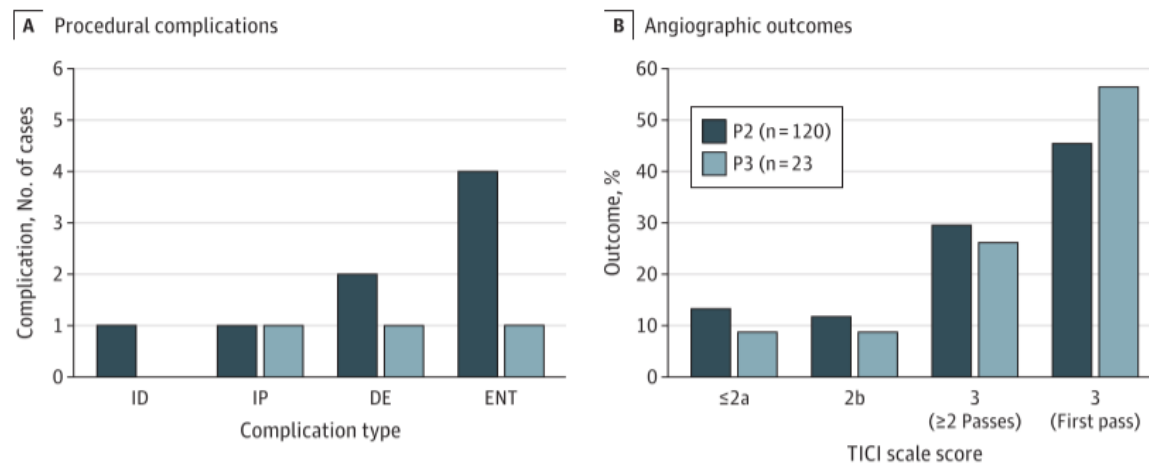
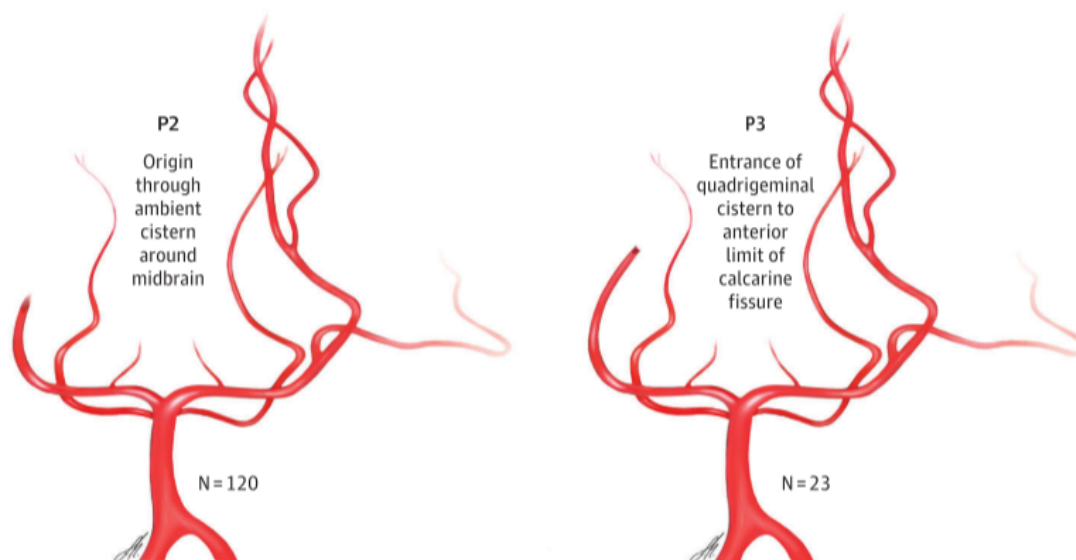
Figure 2. Association of endovascular treatment (EVT) vs medical management (MM) and outcomes expressed as odds ratio (OR) and their 95% CIs, depending on continuous baseline National Institutes of Health Stroke Scale (NIHSS) score.

An OR >1 indicates that the outcome is more likely with EVT, whereas for OR <1 , the outcome is more likely with MM. The outcomes displayed are (A) ordinal modified Rankin Scale (mRS) favorable shift, (B) excellent outcome, (C) functional independence, (D) NIHSS decrease ≥ 2 points, (E) symptomatic intracranial hemorrhage (sICH), and (F) mortality.

Thrombectomy for Primary Distal Posterior Cerebral Artery Occlusion Stroke

The TOPMOST Study

Figure 1. Endovascular Complications and Angiographic Outcomes Stratified by Vessel Segment

**C** P2 and P3 segments

The P2 vessel segment begins from the posterior cerebral artery branch point of the posterior communicating artery, curving around the midbrain within the ambient cistern, to the beginning of the quadrigeminal cistern. The P3 vessel segment begins from the entrance point of the quadrigeminal cistern, through its lateral aspect, to the anterior limit of the calcarine fissure. DE indicates downstream emboli; ENT, emboli to new territory; ID, iatrogenic dissection; IP, iatrogenic perforation; and TICI, Thrombolysis in Cerebral Infarction.

Table 2. Main Outcome and Safety Parameter Compared by Treatment Group Before and After Propensity Score Matching

Outcome	Before PSM			After PSM		
	No. (%)		P value	No. (%)		P value
	Mechanical thrombectomy cohort (n = 143)	Standard medical treatment cohort (n = 100)		Mechanical thrombectomy cohort (n = 92)	Standard medical treatment cohort (n = 92)	
NIHSS score change						
Mean (SD)	−4.0 (6.4)	−2.4 (3.9)	.02 ^a	−3.9 (6.7)	−2.4 (3.6)	.06
Median (IQR)	−3 (−6 to −1)	−1 (−4 to 0)	.005 ^a	−2 (−5 to −1)	−1.5 (−4.2 to 0)	.06
Binary ENI	73 (56.6)	41 (43.6)	.056	36 (42.4)	32 (37.2)	.49
mRS score at 90-d follow-up						
0-1	72 (66.1)	29 (50.9)	.057	51 (66.2)	31 (54.4)	.16
0-2	86 (78.9)	41 (71.9)	.31	59 (76.6)	43 (75.4)	.87
Safety outcomes						
sICH	5 (3.5)	4 (4)	.83	4 (4.3)	4 (4.3)	>.99
Mortality						
In-hospital	7 (5.6)	5 (9.1)	>.99	4 (4.4)	5 (5.4)	>.99
At 90-d follow-up	12 (11)	9 (17.5)	.23	9 (11.8)	9 (15.8)	.40

Abbreviations: ENI, early neurological improvement; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PSM, propensity score matching;

sICH, symptomatic intracerebral hemorrhage.

^a Indicating statistical significance.

Table 1. Summary of evidence from current studies according to arterial localization of the occlusion

Occlusion localization		IVT	EVT
Basilar artery occlusion		Prospective registry data suggest effectiveness especially in severe cases. Similar results to conservative treatment alone in mild-moderate situations.	<i>For moderate to severe cases (NIHSS > 10):</i> RCTs proving effectiveness up to 24 h <i>For mild cases (NIHSS ≤ 10):</i> no sufficient data (neutral results from subgroup analysis of RCTs) No further ongoing RCTs.
Vertebral artery occlusion		Retrospective data suggests that effectiveness is comparable to that of anterior circulation strokes	One retrospective study only suggesting potential harm. No ongoing RCTs.
Posterior cerebral artery occlusion	Included in RCTs demonstrating IVT efficacy in AIS, but likely underrepresented	Overall retrospective analyses suggest improved recanalization rates and numerically improved functional outcome	Retrospective studies only with heterogeneous results. RCTs ongoing.
Cerebellar arteries occlusions		No specific studies, assumptions from posterior circulation overall results	Data from anecdotal cases only. No ongoing RCTs.
Multilevel posterior circulation occlusions		No specific studies, assumptions from posterior circulation overall results	One retrospective study only suggesting similar results to IVT-treated patients. No ongoing RCTs.



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IVT – EVT Protocol Sion 12/2025

Summary



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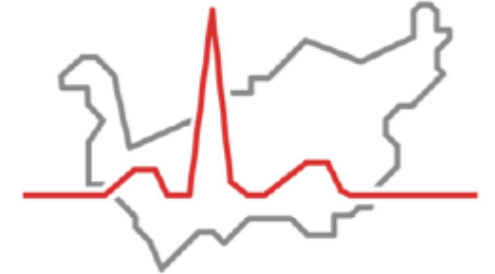
General critiria IVT - EVT

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Service de Neurologie
Unité Cérébrovasculaire du Valais (UCV)

AVC : Protocole TIV-TEV

- Door to CT < 15 min
- Door to TIV < 30 min
- Door-in-door-out < 60 min



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Critères généraux de revascularisation aiguë : TIV et TEV

- AVC ischémique aigu probable selon le neurologue, même si imagerie négative
- NIHSS ≥ 4 selon le neurologue au moment de l'examen
NIHSS < 4 et déficit handicapant (aphasie, hémianopsie, main tombante, diplopie, ...)
Considérer si : - déficit mineur ou régressif avec occlusion proximale (LVO) intracrânienne
- déficit mineur avec occlusion distale et MMR > 1.5 (TIV seule ou DAPT selon situation)
- Bonne qualité de vie : en général mRS ≤ 3 , mais évaluation individuelle ! espérance de vie > 3m
- Critères radiol. : - ACM, ACA, ACP, cervelet : Core (CT natif / ADC noir) < 3/4 du territoire vasculaire
- En général Core total < 150ml
- Pas d'âge limite. Si < 16 ans : contacter neuropédiatre + spécialiste neurovasculaire → protocole AVC péd.

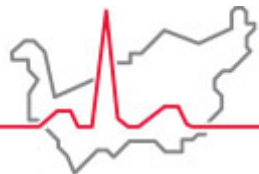


IVT criteria

Critères pour THROMBOLYSE INTRAVEINEUSE (TIV) ± TEV

- ▶ Toutes les situations imposent l'absence de CI absolues ou relatives multiples
- ▶ TIV ≤4.5h avant TEV systématique à l'exception de CI absolue ou CI relatives multiples
- ▶ TIV >4.5h avant TEV est considérée individuellement : délai TEV, DPBS, NIHSS, mRS, âge, CI relatives

Territoire vasculaire	0 – 4.5h depuis DPBS	4.5 – 24h depuis DPBS ou AVC au réveil
ACM	Toujours sauf si CI	Core <70ml ou ASPECTS ≥7 <u>et</u> perfusion MMR ≥1.2 (≥1.8 si >9h) <u>ou</u> DWI+ / FLAIR- mismatch
ACA, ACP, cervelet	Toujours sauf si CI	Core <50% du territoire vasculaire <u>et</u> perfusion MMR ≥1.2
Tronc basilaire (TB)	Toujours sauf si CI	Si DWI+ / FLAIR- mismatch
Lacunes, AChA, no occlusion	Toujours sauf si CI	Si DWI+ / FLAIR- mismatch



EVT criteria

Critères pour THROMBECTOMIE MÉCANIQUE (TEV) ± TIV

► Critère radiologique minimal : Core (CT natif / ADC noir) <3/4 du territoire vasculaire (sauf Siphon et ACM1)

Site d'occlusion *		0 – 24h (48h) depuis DPBS ou AVC au réveil	
Siphon, ACM1		TEV si Core (CT natif / ADC noir) <150ml <u>et</u> ASPECTS ≥3 (sauf si <6h)	
ACM2 ◇	NIHSS ≥8	0 – 8h : TEV	8 – 24h : TEV si MMR ≥1.5
	NIHSS <8	TEV si M2 dominante (ou favorable ≈) <u>et</u> MMR >1.5	
ACP1 ◇, ACA1 ≈ ◇	NIHSS ≥8	0 – 8h : TEV	8 – 24h : TEV si MMR ≥1.5
M3/4, A2/4, P2/4, PICA, AICA, SCA		Pas de TEV	
TB, V4 dominante	NIHSS ≥6 ●	TEV si <u>pas</u> de Core bilatéral étendu tronc/thalamus (IRM/PC-ASPECT)	
Occlusion aiguë <u>extra</u> -crânienne <u>isolée</u> , ou <u>subocclusion</u> <u>intra</u> - ou <u>extra</u> -crânienne		TEV si NIHSS ≥6 ● (éviter TIV si DPBS >4.5h, décider au cas par cas)	

* Si CTA/MRA/DTC indisponible : TEV si artère hyperdense accessible ou si NIHSS ≥8

◇ Discuter avec NRI, plutôt pas de TEV si : TIV possible, patient âgé, mRS ≥3, multiples CI relatives/absolues
≈ TEV possible (voir NRI) si accès peu risqué : tortuosité↓, gros calibre, occlu. prox., déficit significatif, ØTIV

● Discuter avec NRI si NIHSS <6, selon situation



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Thank you