WHAT CAN WE ACHIEVE WITH IV THROMBOLYSIS IN LARGE VESSEL OCCLUSION?

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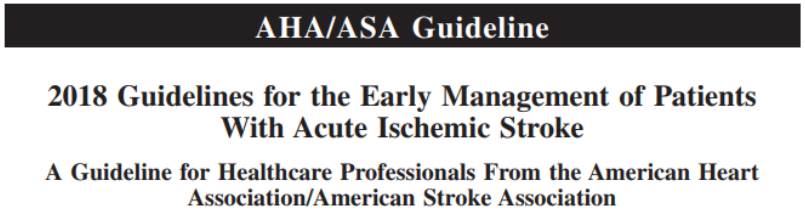
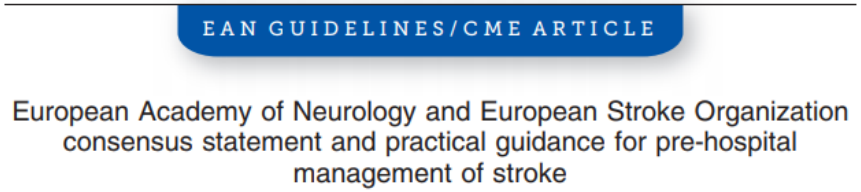
DISCLOSURE STATEMENT OF FINANCIAL INTEREST

I, SHREY MATHUR, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

What can we achieve with IV lysis in LVO and what is the price to pay?

- Intravenous thrombolysis (IVT) with alteplase
  - widely available, approved and guideline recommended systemic treatment associated with improvement of neurological deficit and functional recovery





- Limited by:
  - short time window (4.5 h from stroke onset)
  - several exclusion criteria (including history of recent surgery or anticoagulant intake)
  - frequent re-occlusion (10–25% of the initially re-perfused vessels)
  - poor rates of complete recanalization in large vessel occlusions (LVOs)

Emerging RCT Evidence for MT

- IVT+MT improves outcome in acute anterior circulation stroke patients with proximal vessel occlusion compared to IVT alone
- HERMES collaboration (MR CLEAN, SWIFT-PRIME, EXTEND IA, ESCAPE and REVASCAT, patient-level pooled analysis)
  - similar rates of functional independence and mortality at 90 days between IVT+MT and dMT
  - BUT patients in the direct MT group had contraindications for IV t-PA

Bridging Therapy: Potential Advantages

DISTAL OCCLUSIONS

- IVT pretreatment is highly effective in distal occlusions not accessible by catheters (Seners P, Stroke 2016)

CLOT DETATCHMENT

- tPa induces fibrin degradation which may lead to easier clot detachment during EVT, resulting in higher rates of successful reperfusion with fewer device passes (Grotta JC, Stroke 2015); (Tsivgoulis G, Expert Rev Neurother 2016)

NEW INFARCTION

- tPa pretreatment may reduce the odds of infarction in new (previously unaffected) territory that has been shown to complicate endovascular reperfusion procedures (Ganesh A, ESCAPE Trial, Stroke 2016)

REPERFUSION

- Pretreatment with IVT results in successful reperfusion in 10% of LVO patients eligible for MT obviating the need for endovascular reperfusion procedure (Tsivgoulis G, Stroke 2018)

WORKFLOW

- if rt-PA bolus is delivered CT-scanner with the patient being transferred immediately to the angio-suite where the remaining alteplase infusion will be delivered, there is a significant reduction in unnecessary time delays (Wang H, J SCD, 2017)

Bridging Therapy: Potential Disadvantages

sICH RISK

- sICH in ~6% and major systemic bleeding complications in ~2% (Miller DJ, Neurohospitalist 2011)
- sICH complicated IVT carries high risk of mortality, whereas effective treatment options are still lacking (Yaghi S, JAMA Neurol 2014)

ANAPHYLAXIS

- Angioedema ranging between 1.3-5.1%
- Most cases mild, with no need for ICU support or mechanical ventilation (Censori, Neurol Sci 2018)

DISTAL THROMBUS MIGRATION

- Possible distal thrombus migration resulting in recurrent AIS in the territory of the affected artery

DELAYING EVT

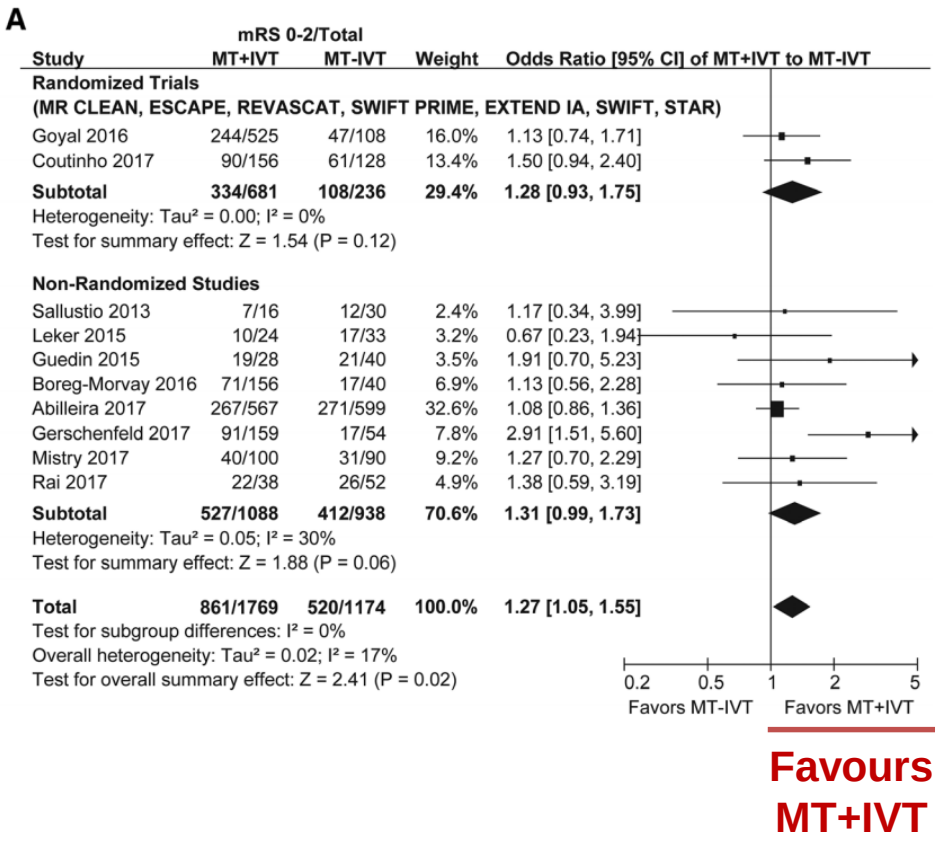
- Possible delay to MT because of delays in arranging IVT

PRECLUDES USE OF HEPARIN/ANTIPLATELETS

- IVT precludes use of heparin and antiplatelets (esp. clopidogrel loading) during the first 24 h following IVT
- May limit the therapeutic options of neurointerventionalists (esp. in patients with tandem extra-cranial and intra-cranial occlusions)

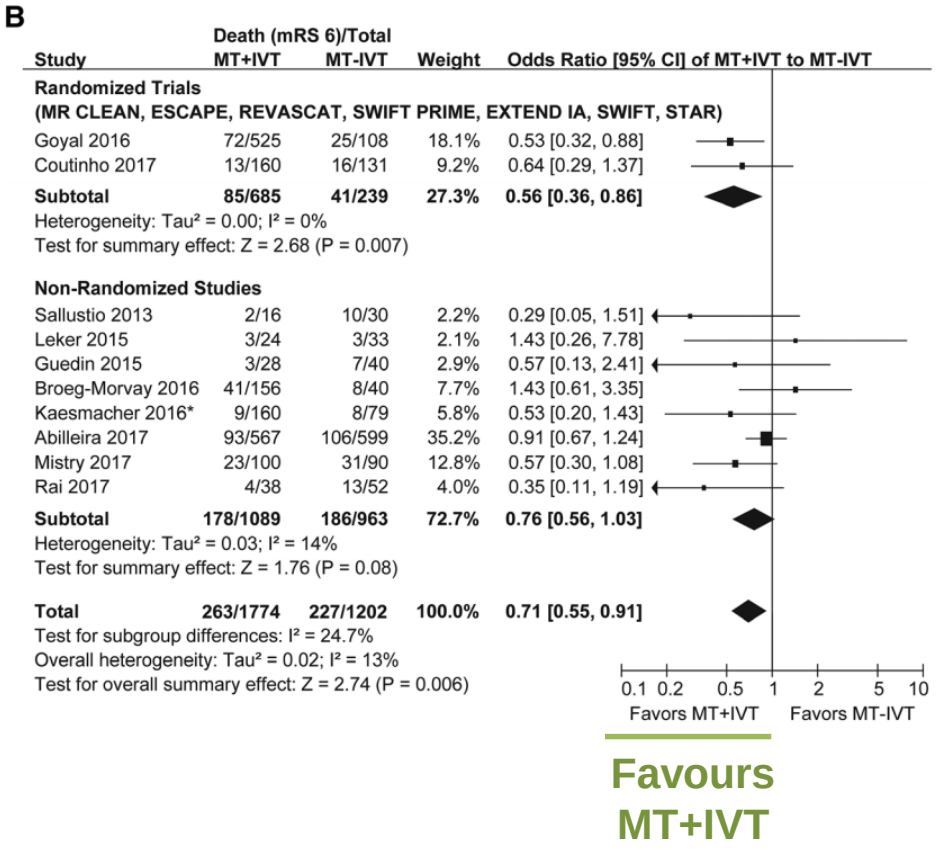
Functional outcomes

mRS 0-2 (good)



Favours MT+IVT

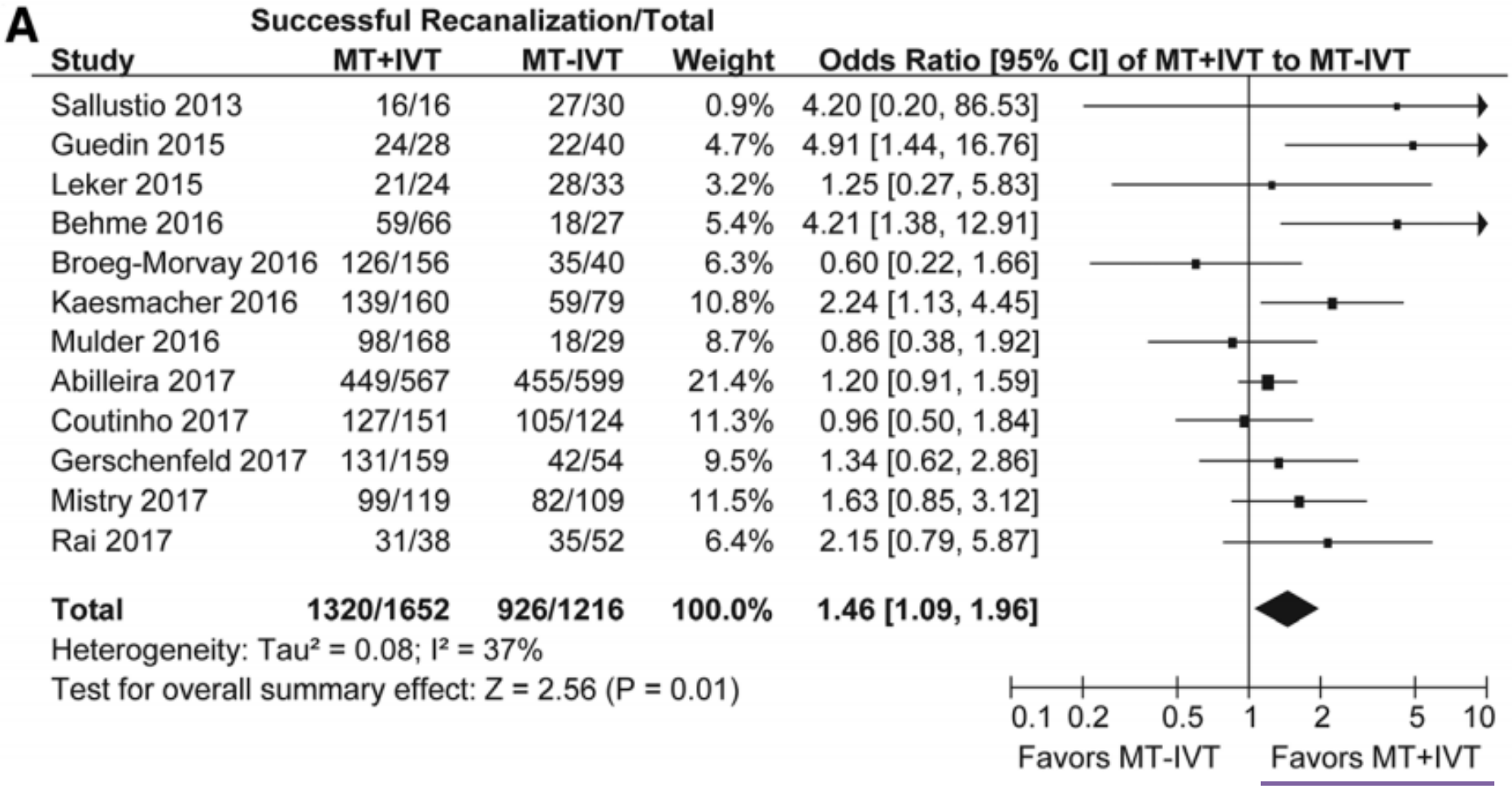
mRS 6 (mortality)



Favours MT+IVT

Mistry et al., Stroke. 2017 Sep;48(9):2450-2456

Successful Recanilisation



Favours MT+IVT

Mistry et al., Stroke. 2017 Sep;48(9):2450-2456

≤2 Device Passes for Successful Recanilisation

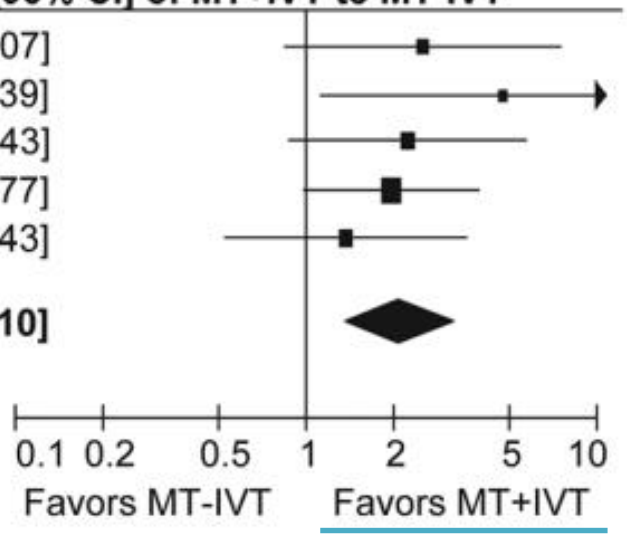
B

≤2 Device Passes for Successful Recanalization/Total

Study	MT+IVT	MT-IVT	Weight	Odds Ratio [95% CI] of MT+IVT to MT-IVT
Guedin 2015	21/28	22/40	14.9%	2.45 [0.85, 7.07]
Leker 2015	21/24	20/33	8.5%	4.55 [1.13, 18.39]
Behme 2016	42/66	12/27	20.1%	2.19 [0.88, 5.43]
Kaesmacher 2016*	47/160	14/79	37.1%	1.93 [0.99, 3.77]
Rai 2017	28/38	35/52	19.4%	1.36 [0.54, 3.43]
Total	**159/316**	**103/231**	**100.0%**	**2.06 [1.37, 3.10]**

Heterogeneity: $Tau^2 = 0.00$; $I^2 = 0\%$

Test for overall summary effect: $Z = 3.48$ ($P = 0.0005$)



Favours MT+IVT

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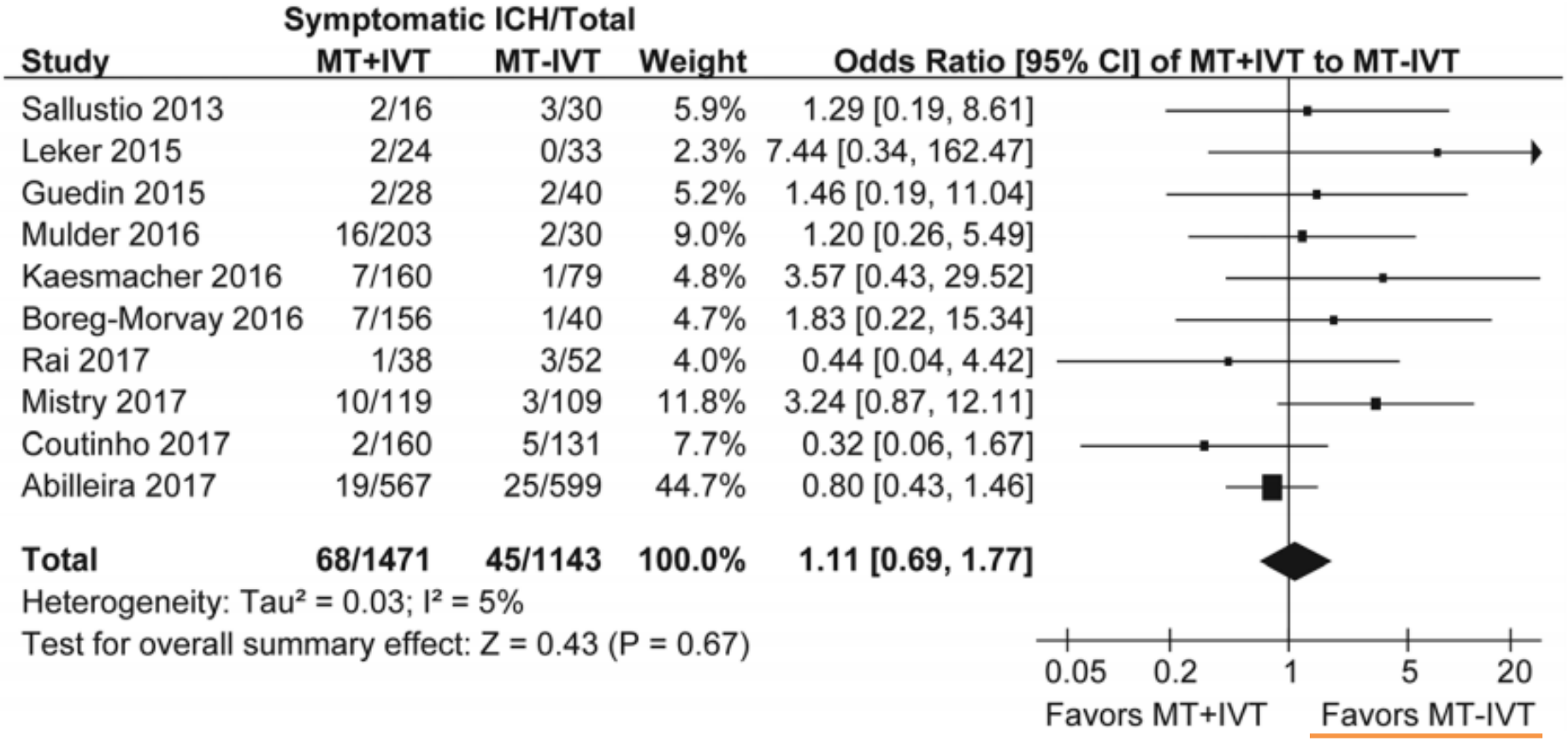
Rates of sICH



Study	Symptomatic ICH/Total MT+IVT	MT-IVT	Weight	Odds Ratio [95% CI] of MT+IVT to MT-IVT
Sallustio 2013	2/16	3/30	5.9%	1.29 [0.19, 8.61]
Leker 2015	2/24	0/33	2.3%	7.44 [0.34, 162.47]
Guedin 2015	2/28	2/40	5.2%	1.46 [0.19, 11.04]
Mulder 2016	16/203	2/30	9.0%	1.20 [0.26, 5.49]
Kaesmacher 2016	7/160	1/79	4.8%	3.57 [0.43, 29.52]
Boreg-Morvay 2016	7/156	1/40	4.7%	1.83 [0.22, 15.34]
Rai 2017	1/38	3/52	4.0%	0.44 [0.04, 4.42]
Mistry 2017	10/119	3/109	11.8%	3.24 [0.87, 12.11]
Coutinho 2017	2/160	5/131	7.7%	0.32 [0.06, 1.67]
Abilleira 2017	19/567	25/599	44.7%	0.80 [0.43, 1.46]
Total	**68/1471**	**45/1143**	**100.0%**	**1.11 [0.69, 1.77]**

Heterogeneity: Tau² = 0.03; I² = 5%

Test for overall summary effect: Z = 0.43 (P = 0.67)

Favours MT+IVT

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SWIFT DIRECT

- Awaiting RCT (SWIFT DIRECT) to assess whether dMT is equally effective as IVT+MT (bridging thrombolysis)
- 30+ centers, more than 400 subjects
- Estimated Study Completion Date: December 31, 2021

- SWIFT DIRECT may have implications for changing acute stroke management
  - If dMT is non-inferior to bridging thrombolysis, then dMT would be therapy of choice in CSC
  - trial does not address whether patients arriving in PSCs should be pre-treated with IV t-PA or whether they should directly be referred to CSCs

Conclusions

- Evidence from Meta-Analysis
  - MT+IVT patients had **better functional outcomes**, **lower mortality**, **higher rate of successful recanalization**, **requiring fewer device passes**, and **equal odds of sICH** compared with MT-IVT patients
- IVT and MT should be regarded as two highly effective and complementary reperfusion therapies
  - LVO patients (with no CI to IVT) should receive IVT ASAP followed by immediate transfer to the cath lab for prompt MT initiation
- Limitations and Future Research
  - Data from studies where MT+IVT and MT−IVT groups differ based on IVT eligibility
  - Comparison in studies with matched ages, baseline NIHSS, and symptom onset to groin puncture time between MT+IVT and MT−IVT groups failed to demonstrate a significant difference
  - Require RCTs directly comparing bridging therapy with MT (SWIFT DIRECT)

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তোমাকে ধন্যবাদ
감사합니다
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