

Changing Paradigms: Should we go direct to thrombectomy ?

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Objectives

Review recent literature regarding

1. Among patients with acute ischemic stroke secondary to LVO and eligible for thrombolysis, should we skip intravenous thrombolysis and go directly for mechanical thrombectomy?
2. Should we bypass a closer primary stroke center and go directly to a thrombectomy capable center in patients with a stroke with suspicion of a LVO in the field

Background

Multiple RCTs have consistently demonstrated that patients with a LVO in the anterior circulation benefit from EVT following IVT

Is intravenous thrombolysis needed in combination with mechanical thrombectomy in patients with acute LVO stroke?

IV Thrombolysis in LVO

Potential benefits:

- Contribute to reperfusion, averting the need for EVT
- Promote dissolution of downstream micro emboli improving distal perfusion

Potential risks:

- Increase the risk of intracranial or systemic hemorrhage
- Lead to thrombus fragmentation and worsening distal perfusion
- Delay the start of the endovascular treatment.
- Limits the use of antithrombotic therapy within 24-hour
- Increases health care costs

Known low recanalization rates in LVO, especially ICA

Should we SKIP IV and go DIRECT-MT

SKIP (Japan)

DIRECT-MT (China)

DEVT (China)

MR CLEAN NO-IV (Netherlands, Belgium, France)

Inclusion Criteria

Patients that could be treated with IVT < 4.5 hours

Mothership

Alteplase dosing: SKIP 0.6mg/kg
(others standard dosing of 0.9mg/kg)

Vessel occlusion: DIRECT-MT -ICA, M1 and proximal M2
(others ICA, M1)

Trial design: MR CLEAN NO-IV – superiority
(others non-inferiority)

90 day mRS 0-2

	dEVT	Combined	Non-inferiority
SKIP 103/101	59.4%	57.3%	P=0.18
DIRECT-MT** 327/329	36.4%	36.8%	P=0.04
DEVT 116/118	54.3%	46.6%	P=0.003

Symptomatic ICH

Mortality-90 day

	dEVT	Combined
SKIP	5.9%	7.8%
DIRECT-MT	4.3%	6.1%
DEVT	6.1%	6.8%

	dEVT	Combined
SKIP	7.9%	8.7%
DIRECT-MT	17.7%	18.8%
DEVT	17.2%	17.8%

eTICI \geq 2b

Door to Puncture

	dEVT	Combined
SKIP	90.1%	93.2%
DIRECT-MT	79.4%	84.5%
DEVT	88.5%	87.2%

	dEVT	Combined
SKIP**	20 min	22 min
DIRECT-MT	84 min	85.5 min
DEVT	101 min	105 min

MR CLEAN NO-IV

	Allocated to direct EVT N-273 Ordinal mRS	Allocated to alteplase 0.9mg/kg + EVT N-266 Ordinal mRS	P value
Primary analysis: ordinal mRS	Overall acOR > Does not show dichotomizations		acOR 0.88 (95% CI 0.65-1.19)
Secondary Outcomes Symptomatic ICH (safety)	16 (5.9%)	14 (5.3%)	1.30 (0.61-2.84)
Mortality (Safety)	56 (20.5%)	42 (15.8%)	1.39 (0.84-2.30)

Pooled data

SHRINE collaboration- SKIP + DEVT
Noninferiority analysis

90d mRS 0-2: dEVT vs Combined: aOR 1.27 (95% CI, 0.84 - 1.92)

Prespecified lower noninferiority boundary of 0.85 and therefore cannot fully confirm the noninferiority of direct thrombectomy

Symptomatic ICH: dEVT vs Combined 6.5% vs 9.0%; $P = 0.49$
Any ICH: dEVT vs Combined 26.3% vs 39.4%; $P = 0.004$

Survival 90 day- 87% in both groups

Pooled data

SKIP + DIRECT-MT + DEVT + MR CLEAN-NO IV

No difference between approaches for achievement of functional independence (mRS 0 to 2) at 90 days (OR 1.04; 95% CI 0.83-1.29).

So what does this mean?

Direct thrombectomy is not superior to a combined approach

Direct thrombectomy may be non-inferior to a combined approach

Ongoing trials
SWIFT-DIRECT
DIRECT-SAFE

So what does this mean?

Does not change practice for a drip and ship model

For patients presenting directly to thrombectomy capable center with rapid work flows and immediate availability of endovascular service

Should we be giving IV alteplase to all LVO patients, or are there subgroups who benefit from bridging

Personalized approach

If any doubt regarding IV TPA contraindications or higher bleeding risk, then can SKIP thrombolysis

?Subgroups
> 3 hours from symptom onset
Intracranial ICA occlusion
Atrial fibrillation

? Cost

Optimal transfer paradigm for ELVO

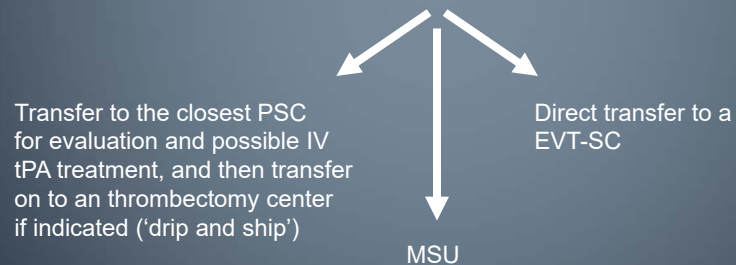
Outcome after ischemic stroke is heavily dependent on time from onset of symptoms to reperfusion therapy, regardless of therapy

Imperative that stroke systems of care rapidly identify symptomatic patients, and reduce time from onset to definitive treatment

Optimal transfer paradigm for ELVO

Significant proportion of the population is not directly served by a thrombectomy capable center

For patients who display symptoms suggesting an ELVO when assessed in the field by EMS



RACECAT trial

Catalan territory of Spain X 3 years

Stroke and suspected ELVO (RACE ≥ 5)

Located in geographical areas not covered by an EVT-SC

Estimated arrival at an EVT-SC within 7 hours of onset

RACECAT

	PSC	EVT-SC	P
LVO	65%	69%	
IV TPA	60%	48%	< 0.001
Onset to needle (Median, min)	120	155	< 0.001
EVT (+/- TPA)	41%	50%	0.003
Onset to puncture (Median, min)	270	214	< 0.001

RACECAT

Primary efficacy outcome (strokes/TIA)
90 day mRS was comparable in the EVT-SC and PSC groups
(adOR odds 1.02, 95% CI 0.8 to 1.2)

Primary safety outcome
Overall mortality and mortality in ICH patients were comparable

Negative for the primary efficacy endpoint; a mothership transfer protocol in patients with suspected ELVO did not prove superior to the drip and ship protocol.

Implications for triage

RACECAT trial indicates that direct transfer to an EVT-SC for ELVO strokes with a RACE scale ≥ 5 is not associated with better outcomes if the median time difference between the mothership and 'drip and ship' paradigms is less than 60 min.

May be of benefit

Slower work flow at PSCs

Longer inter-hospital travel times due to resource or logistics limitations

TRIAGE-STROKE trial

Future modifiers of stroke for triage

Technology

MSU

TCD, VIPS

AI

Thrombolysis

IV Tenecteplase

Neuroprotection

Nerinetide

SPG stimulation

Conclusions

IV thrombolysis remains standard of care in acute ischemic stroke with LVO and should be given in eligible patients prior to thrombectomy

Future trials may identify LVO subgroups where IV thrombolysis can be skipped and can proceed directly to thrombectomy, especially in a mothership model

Each region should explore and understand their systems of care better to optimize stroke triage protocols for ELVO

Thank you

