

The patients selection is a key

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DISCLOSURE STATEMENT OF FINANCIAL INTEREST

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

AFFILIATION/FINANCIAL RELATIONSHIP

- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

COMPANY

- Medtronic
- Bayer, Boehringer Ingelheim, Pfizer, Daiichi Sankyo
i-MHS, CLP
- HOT-TIA
- HOT-TIA
- HOT-TIA

DISCLOSURE STATEMENT OF FINANCIAL INTEREST

I, (Devesh Sinha) 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.

Clinicians Brain Selection Process

- Man aged 70
- Symptoms onset 40 mins
- No risk factors
- Severe ischaemic stroke NIHSS of 22
- ASPECTS of 7
- M1 occlusion
- No collaterals
- At CSC 40 min to groin from onset
- Will he benefit from MT?

- Woman aged 80
- Too late for tPA
- DM and high BP
- NIHSS score of 22
- ASPECTS of 9
- Carotid T occlusion
- Good collaterals
- Should she be transferred to 1 hours away if MT is just possible within the 8 hour?

IMS to HERMES- Patients selection

- 2013 IMS III, MR RESCUE, SYNTHESIS –
- No benefit of MT compared to tPA
- However these trials had many issues:
 - First-generation endovascular devices with low recanalization rates
 - The time window from symptom to revascularization was substantial
- Vessel imaging prior to randomization was not mandatory.

Unselected or Highly selected patients

- Among the 10 eligible RCT, 5 studies reported the use of advanced imaging.
- Advanced imaging compared with studies using conventional neuroimaging
 - Higher treatment effects on 3-month Functional independence (odds ratio -3.79)
 - Favourable functional outcome (odds ratio - 3.16)
- The rate of successful reperfusion was higher in studies with advanced imaging
- No difference in the mortality and SICH rates was found between the 2 groups.
- Advanced Neuroimaging in Stroke Patient Selection for Mechanical Thrombectomy, A Systematic Review and Meta-Analysis Georgios Tsivgoulis Stroke. 2018;49:3067–3070

Patient Selection Determinants

1. Age
2. Baseline NIHSS score
3. Systolic Blood pressure
4. Treatment with intravenous tPA
5. History of ischaemic stroke
6. Atrial fibrillation
7. Diabetes mellitus
8. Pre-stroke mRS score
9. ASPECTS
10. Location of occlusion
11. Collateral score
12. Time to treatment
13. Corresponding interactions with treatment

Patients Selection- Clinical decision tool

- Selection of individual patients for MT should not be based on single patient characteristics
- Few clinical decision tool combines multiple clinical and radiological characteristics and shows large variations in treatment benefit
- This modelling tool of individualised selection of patients for MT for AIS and may be used as tool for assisting clinical decision making, consent
- Data from the MR CLEAN and validated in patients in the IMS-III Trial
- https://mrpredicts.shinyapps.io/RRRR_1/
- Selection of patients for intra-arterial treatment for acute ischaemic stroke: development and validation of a clinical decision tool in two randomised trials Esmee Venema, BMJ 2017;357:j1710

A stylised representation of the clinical decision tool.

Patient 1

MR PREDICTS

Clinical decision tool for intra-arterial treatment in acute ischaemic stroke

Patient characteristics

Age (years)
70

NIHSS
22

Pre-stroke mRS
0

Previous stroke
No

Diabetes mellitus
No

Systolic blood pressure (mm Hg)
140

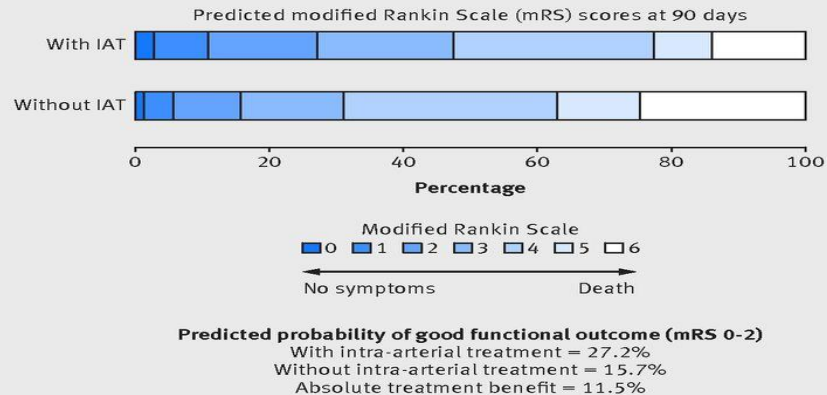
Intravenous tPA
Yes

ASPECT score
10

Location of occlusion
☒ Intracranial ICA (with or without M1)
☐ M1 only
☐ M2 only

CTA collateral score
☒ 0 - absent collaterals
☐ 1 - poor (<50% filling)
☐ 2 - moderate (>50% filling)
☐ 3 - good collaterals

Estimated time from onset to groin puncture (minutes)
100



Patient 2

MR PREDICTS

Clinical decision tool for intra arterial treatment in acute ischaemic stroke

Patient characteristics

Age (years)
80

NIHSS
22

Pre-stroke mRS
0

Previous stroke
No

Diabetes mellitus
Yes

Systolic blood pressure (mm Hg)
180

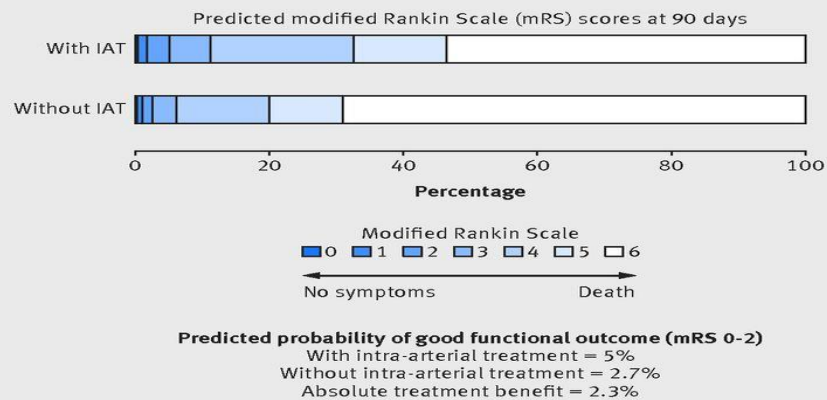
Intravenous tPA
No

ASPECT score
10

Location of occlusion
☒ Intracranial ICA (with or without M1)
☐ M1 only
☐ M2 only

CTA collateral score
☒ 0 - absent collaterals
☐ 1 - poor (<50% filling)
☐ 2 - moderate (>50% filling)
☐ 3 - good collaterals

Estimated time from onset to groin puncture (minutes)
350



Esmee Venema et al. BMJ 2017;357:bmj.j1710

Patients selection at individualised level

MR PREDICTS

Clinical Decision Tool for Intra-Arterial Treatment in Acute Ischemic Stroke

Patient characteristics

Age (years)

60

ASPECT score

0

10

NIHSS

10

Pre-stroke mRS

1

Previous stroke

No

Diabetes mellitus

Yes

Systolic blood pressure (mmHg)

120

Intravenous tPA

Yes

Location of occlusion

☐ Intracranial ICA (with or without M1)

☒ M1 only

☐ M2 only

CTA collateral score

☐ 0 - absent collaterals

☐ 1 - poor (<50% filling)

☐ 2 - moderate (>50% filling)

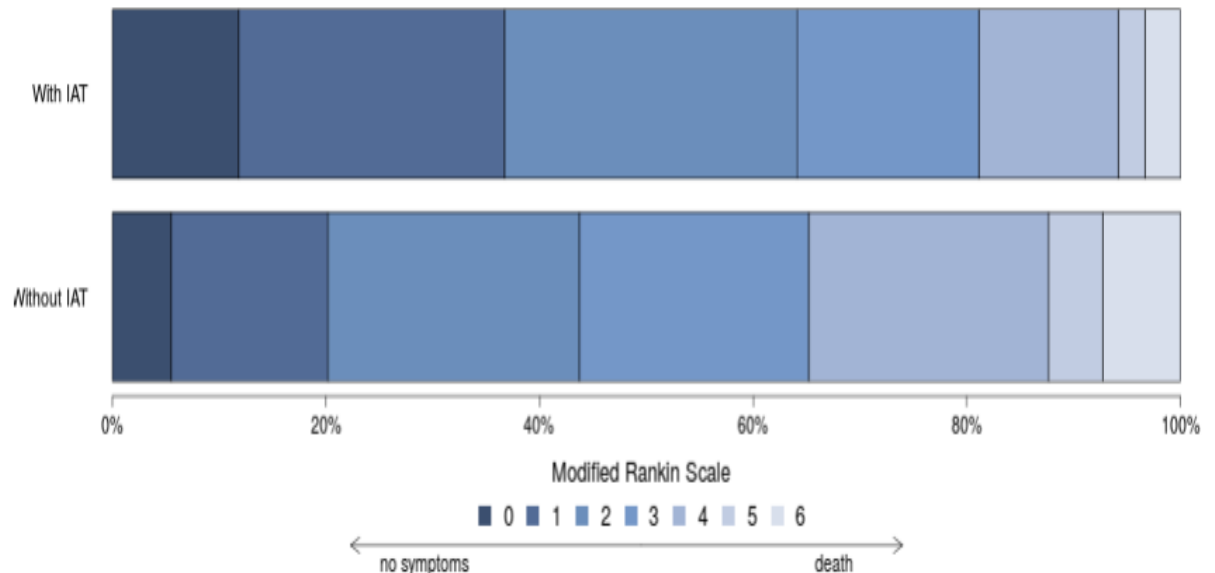
☒ 3 - good collaterals

Estimated time from onset to groin (minutes)

240



Predicted modified Rankin Scale (mRS) scores at 90 days



Predicted probability of good functional outcome (mRS 0-2)

With intra-arterial treatment = 64.1 %

Without intra-arterial treatment = 43.7 %

Absolute treatment benefit = 20.4 %

Getting somewhere in Patient selection

- Either PSC or CSC, proceeding with thrombectomy incurs substantial costs because resources are potentially diverted from other patients.
- To maximise benefit and minimise both harm and costs, it is important to identify those for whom this invasive treatment would be futile or harmful.
- GMC Good practice – Patient / Next of Kin need to be informed.

Patients Selection- Tissue window

- Region of brain that was poorly perfused but not yet infarcted.
- The usual 6-hour “time window” for stroke treatment is there to be replaced with a “tissue window.”
- NHS England- Up to 12 hours

What about Tissue window in MT?

- DAWN trial, the patients had larger penumbral regions, which reflected the requirement for occlusion of a large cerebral vessel.
- Indirect comparisons indicate that AIS patient selection for MT using advanced imaging appears to be associated with improved clinical outcomes.
- The use of advanced neuroimaging for both the selection and prediction of prognosis for MT should not depend on the elapsed time from onset.

What about Tissue window in t-PA?

- Two randomized trials of intravenous thrombolysis that required evidence of penumbral tissue on imaging studies had strikingly negative outcomes
 - Probably because the patients had only small infarct cores and small penumbral regions, which generally would not be expected to improve with recanalization.
-
- Hacke W, Furlan AJ, Al-Rawi Y, et al. Intravenous desmoteplase in patients with acute ischaemic stroke selected by MRI perfusion–diffusion weighted imaging or perfusion CT (DIAS-2): a prospective, randomised, double-blind, placebo-controlled study. *Lancet Neurol* 2009;8:141-50.
 - Albers GW, von Kummer R, Truelsen T, et al. Safety and efficacy of desmoteplase given 3-9 h after ischaemic stroke in patients with occlusion or high-grade stenosis in major cerebral arteries (DIAS-3): a double-blind, randomised, placebo-controlled

“Imaging is the brain”

- CT, CTA and CTP - rapid, reliable information about stroke pathophysiology
- Multimodal CT - treatment responders for both iv thrombolysis and MT
- Trial results and previous studies validating the use of multimodal imaging
- In the era of MT, the use of multimodal imaging routinely to guide treatment can no longer be avoided.
- There is now a strong rationale for multimodal CT before treatment as a standard of care for all patients.

Best outcome – Early

- The results of the DAWN trial do not support a general liberalization of the time window for MT or tPA.
- Reducing the time from the onset of stroke to treatment remains essential and results in the best outcomes.
- A limited proportion of patients with occlusion of a large vessel who present late after the onset of stroke will have a mismatch.

Determinants for patient selection

1. Baseline NIHSS score
2. Pre-stroke mRS score
3. ASPECTS
4. Location of occlusion
5. Collateral score
6. Time to treatment
7. Penumbra volume and mismatch ratio

1. Age
2. Systolic Blood pressure
3. Treatment with IV tPA
4. History of ischaemic stroke
5. Atrial fibrillation
6. Diabetes mellitus
7. Corresponding interactions with treatment

Counting.....

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