Interventional Treatment in the Setting of Low ASPECTS Score

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Disclosures

No financial conflicts to disclose

Endovascular treatment of large core infarcts discussed (off-label use of devices)

Goal of Acute Stroke Care

- A good functional recovery is always the goal of stroke care
- Working backwards:
  - Permanent deficits are correlated with size of stroke
  - Size of stroke is correlated with duration of large vessel occlusion
  - Size of stroke is inversely correlated with degree of collateral flow into ischemic bed.

  - Graphic growing infarct
  - Comparison graphic infarct growing slowly against collaterals.
  - Factors for collaterals: long standing stenosis HTN Against age, proximal occlusion, hypotension, anesthesia

Adding graphic here.

What we know from randomized controlled trials

- IV TPA is safe and effective in treating ischemic stroke given within 3 hours of onset. NNT
- Thrombectomy is safe and effective in treating ischemic stroke with last known well (LKW) < 24 hours provided minimal ischemic changes are present on neuro imaging
  - Meta-analysis of 1764 patients in randomized trials 2010-2017 show a shift to better outcome in thrombectomy patients with odds ratio of 2.0
- Prove that shortening time the reperfusion gives better outcomes

Lancet Neurol 2018; 17: 895–904

Frontier Stroke Therapy

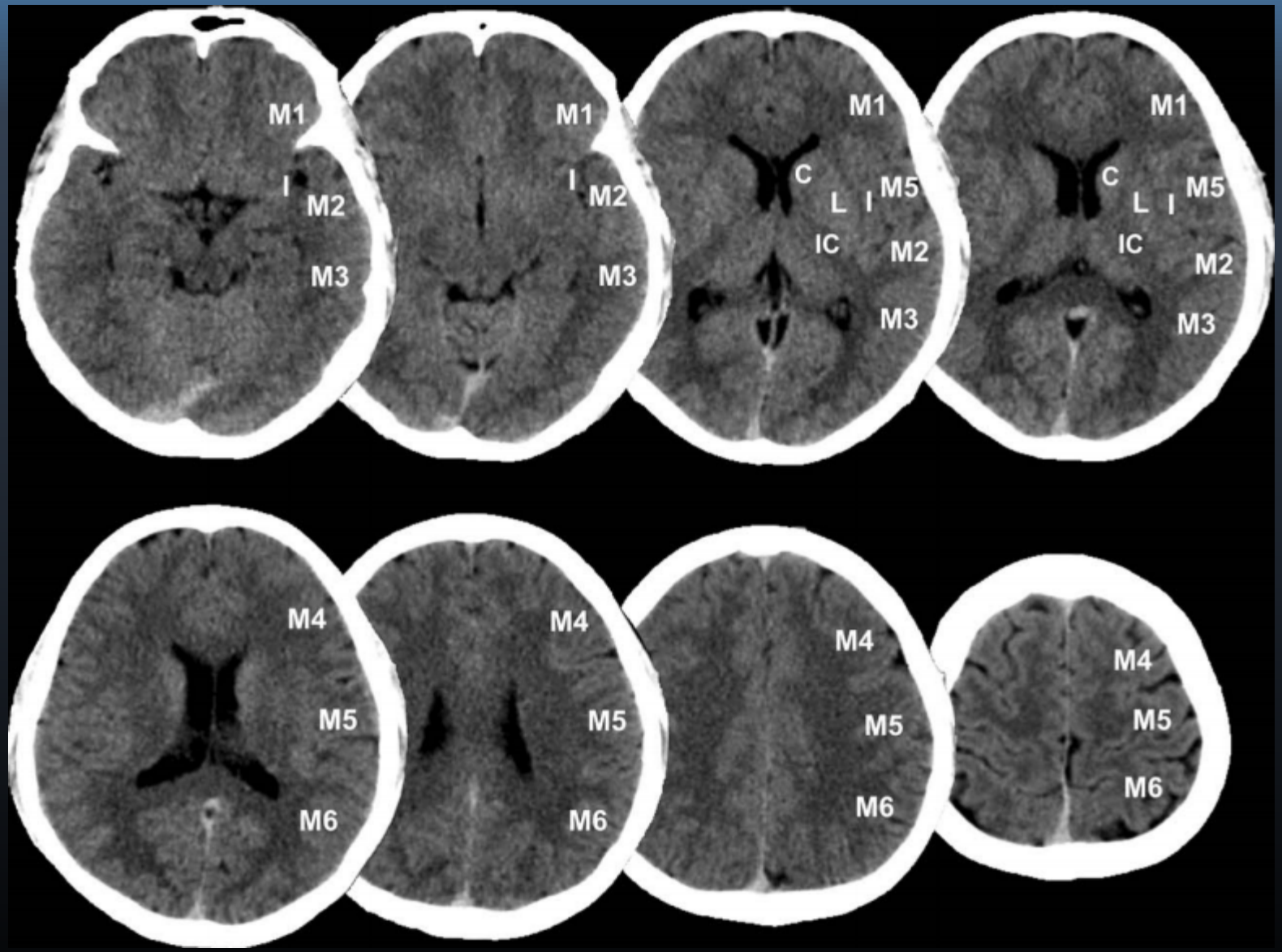
- RCT have been limited to patients with minimal ischemic burden on imaging.
- So far trials seeking to extend indications have been successful.
- How far can we go?

Means of identifying ischemic burden

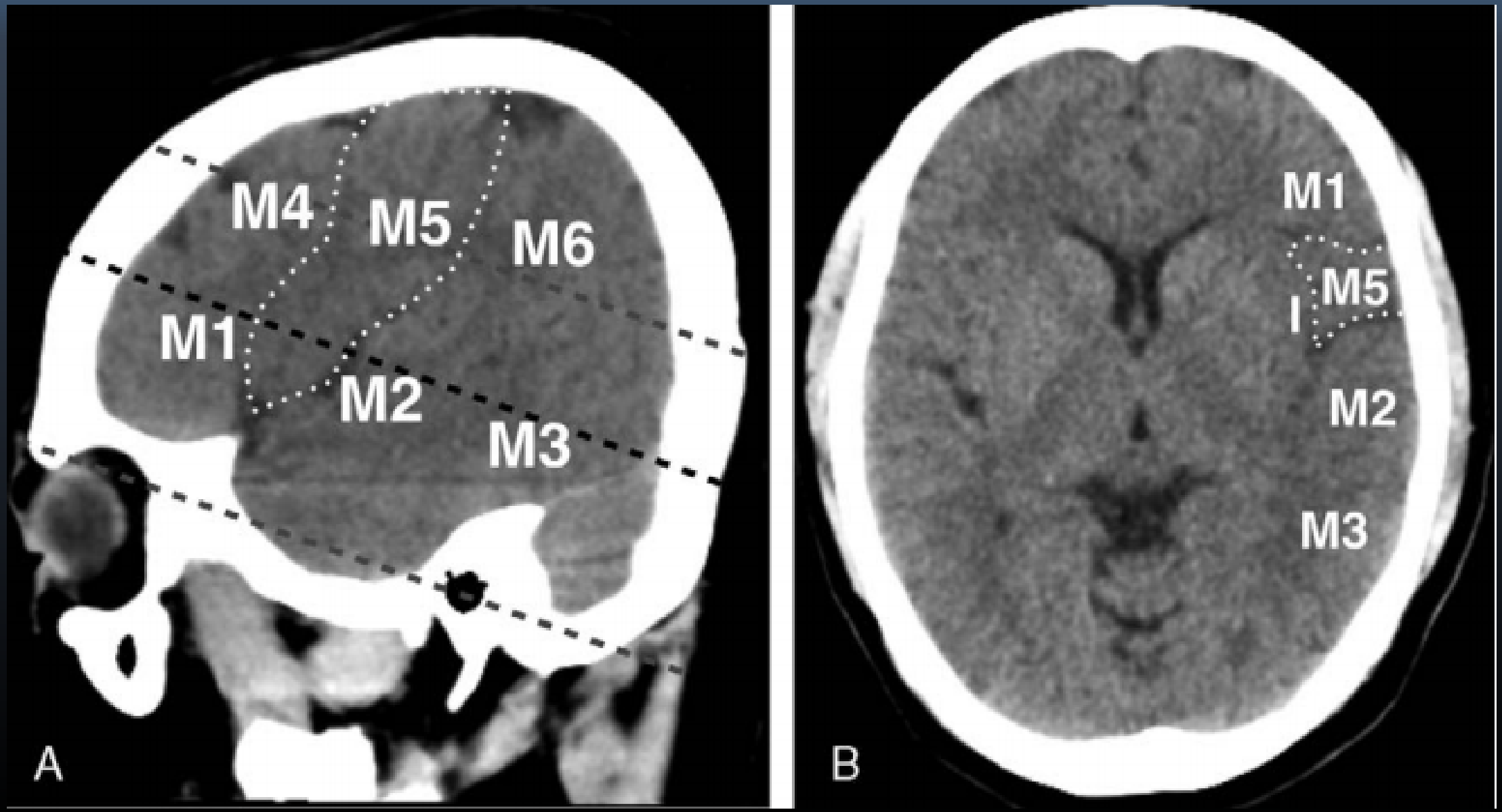
- ASPECTS (Alberta Stroke Program Early CT Score) Standardized reading of non-contrast head CT
- Perfusion Scans: Contrast enhanced scan with calculated flow of contrast through brain tissue.
- Both techniques are quantitate

ASPECTS

- Provides a score for the size of a hemispheric stroke.
- Identifies 10 brain regions. Normal brain scores 10. Patient loses one point for each area showing any ischemic change



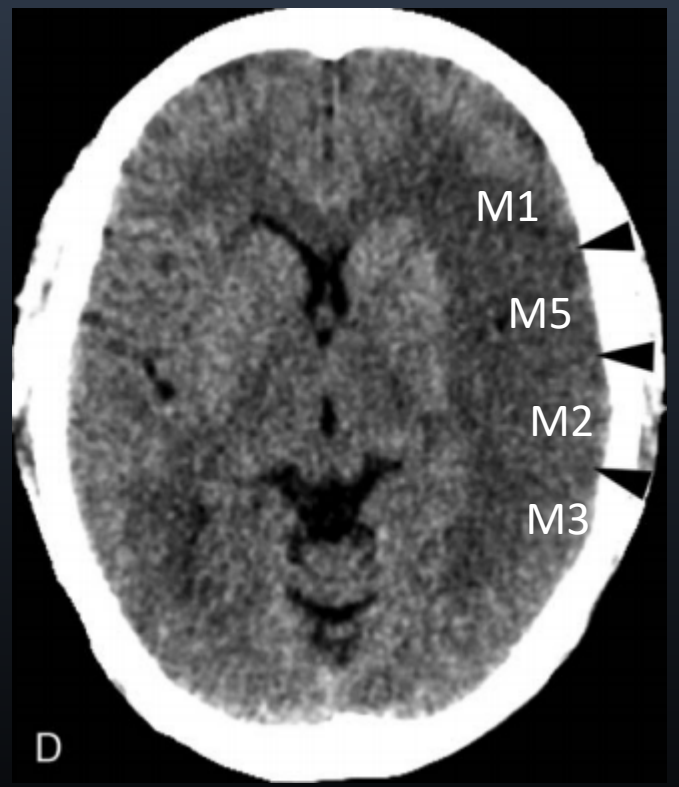
Topics in Magnetic Resonance Imaging Volume 26, Number 3, June 2017


M4
M5
M6
M1
M2
M3
A
M1
M5
I
M2
M3
B

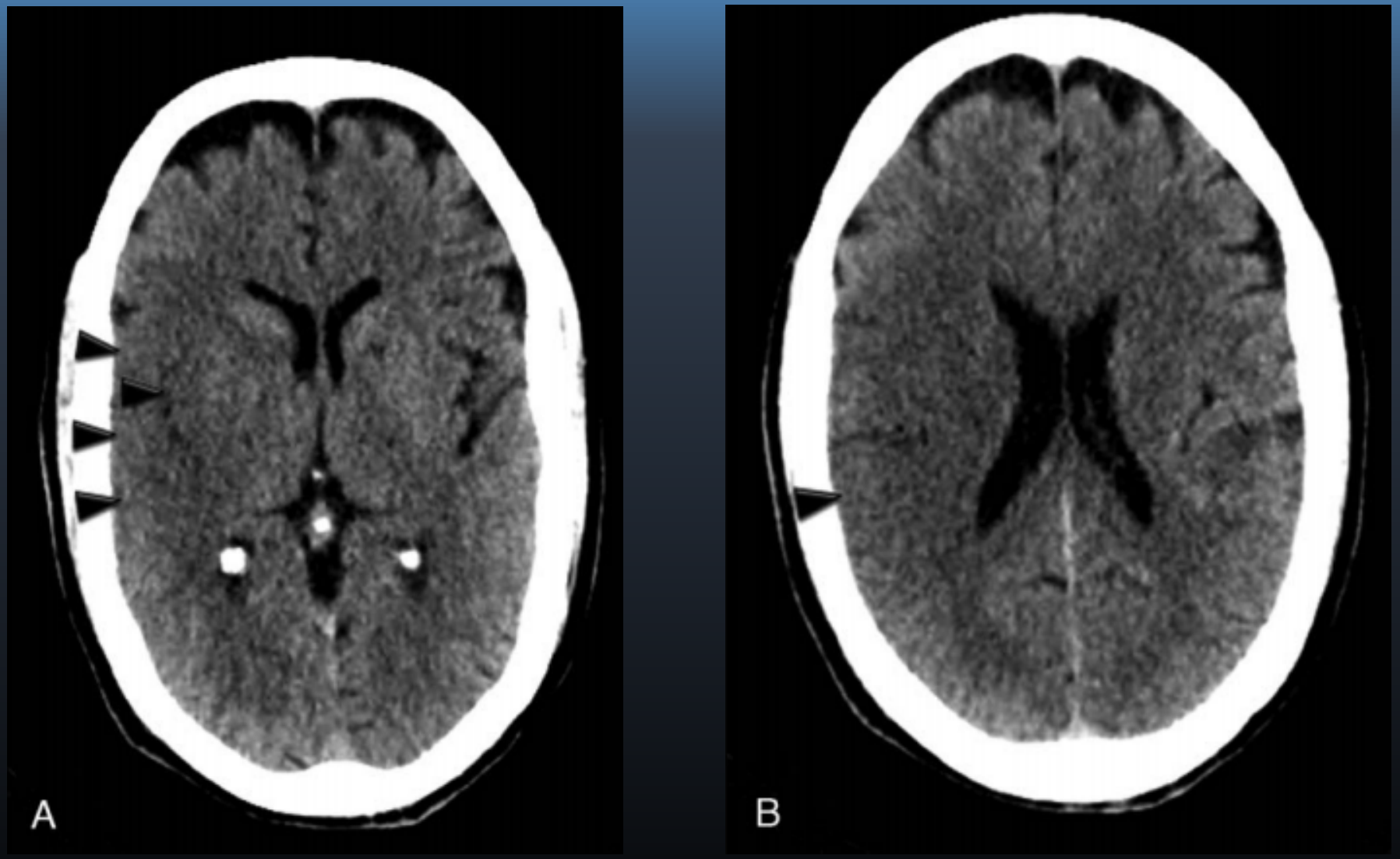
35 year old with stroke ASPECTS = 6.

Scan at 1 Hour

Scan at 2 Hours



Scan at 8 Hours



59 year old man with CT scan 3.5 hrs after stroke onset. Loss of grey white differentiation, cortical hypodensity and sulcal effacement

ASPECTS Utility

- Low scores = many cortical zones infarcting.
  - Example ASPECTS=3 is calculated 10 – 7 infarct areas.
- Very low aspects scores are caused by ICA and M1 occlusion
- Low scores prognosticate disability
- Low scores predict higher hemorrhage rates post TPA though TPA remains beneficial overall.
- High aspect scores predict good recovery

ASPECTS Limitations

- Poor interrater reliability in first 90 minutes of stroke
- Requires training (preferably certification) of reading staff.
- Parenchymal hypodensity is from smaller old infarcts confuses scoring.
- Subjective to artifacts in patients with good mineralization of skull
- Not inclusive of posterior circulation strokes

e-ASPECTS

- Machine learning algorithms can process non contrast head CT and render ASPECTS score at non-inferior accuracy to neuroradiologists
- Software available as add on to existing stroke CT imaging packages
- Particularly valuable for low volume centers where radiologist sub specialization not present.

International Journal of Stroke 2017, Vol. 12(6) 615–622

ASPECTS as Applied to Thrombecotmy Trials

- Randomized controlled trials (MR CLEAN, EXTEND IA, ESCAPE, SWIFT PRIME, REVASC) sought to increase the odds of a positive result by enriching the study population with favorable ASPECTS score patients.
- Patients with scores below 6 or 7 were excluded from study

Relationship between ASPECTS and MRI Infarct Volume

- Infarct volume on DWI MRI is easy to measure (formula ABC/2)
- Infarcts > 100 ml have > 90% specificity for poor outcomes at 90 day (mRS 3-6)
- ASPECTS scores 0-3 are very likely to have an acute infarct volume > 100ml (Sensitivity 77% specificity 97%) J Neuroimaging 2011;21:229-231.
- Successful treatment of low ASPECTS would be a major innovation.

Perfusion Scanning

- Performed with either CT or MRI
- Creates a “movie” of enhanced bloodflow through brain tissue showing the effect of a blockage slowing or stopping flow to tissue.
- Movie is converted to color maps showing
  - Cerebral blood flow
  - Cerebral blood volume
  - Average transit time
  - Time to maximum bolus peak

Stroke. 2020;51:1017-1024. D

CT Versus MRI Perfusion

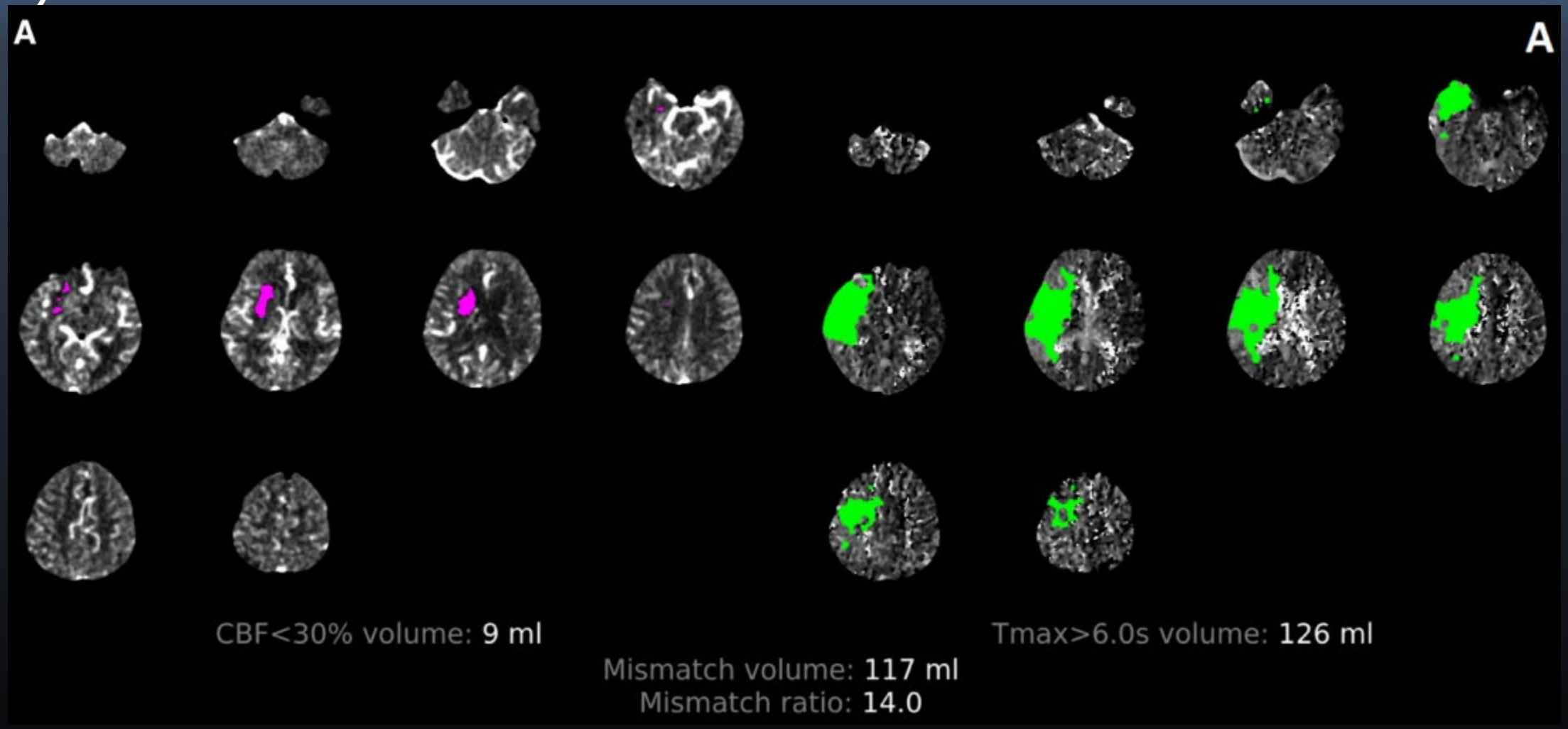
Computed tomography perfusion imaging	Magnetic resonance perfusion imaging
Radiation required	No radiation required
Lower signal-to-noise ratio	Higher signal-to-noise ratio
Indirect estimation of ischemic core	Direct visualization of infarction
Iodine contrast-related complications	Gadolinium retention
Less contraindications	More contraindications
Readily available	Limited availability

Stroke. 2020;51:1017–1024

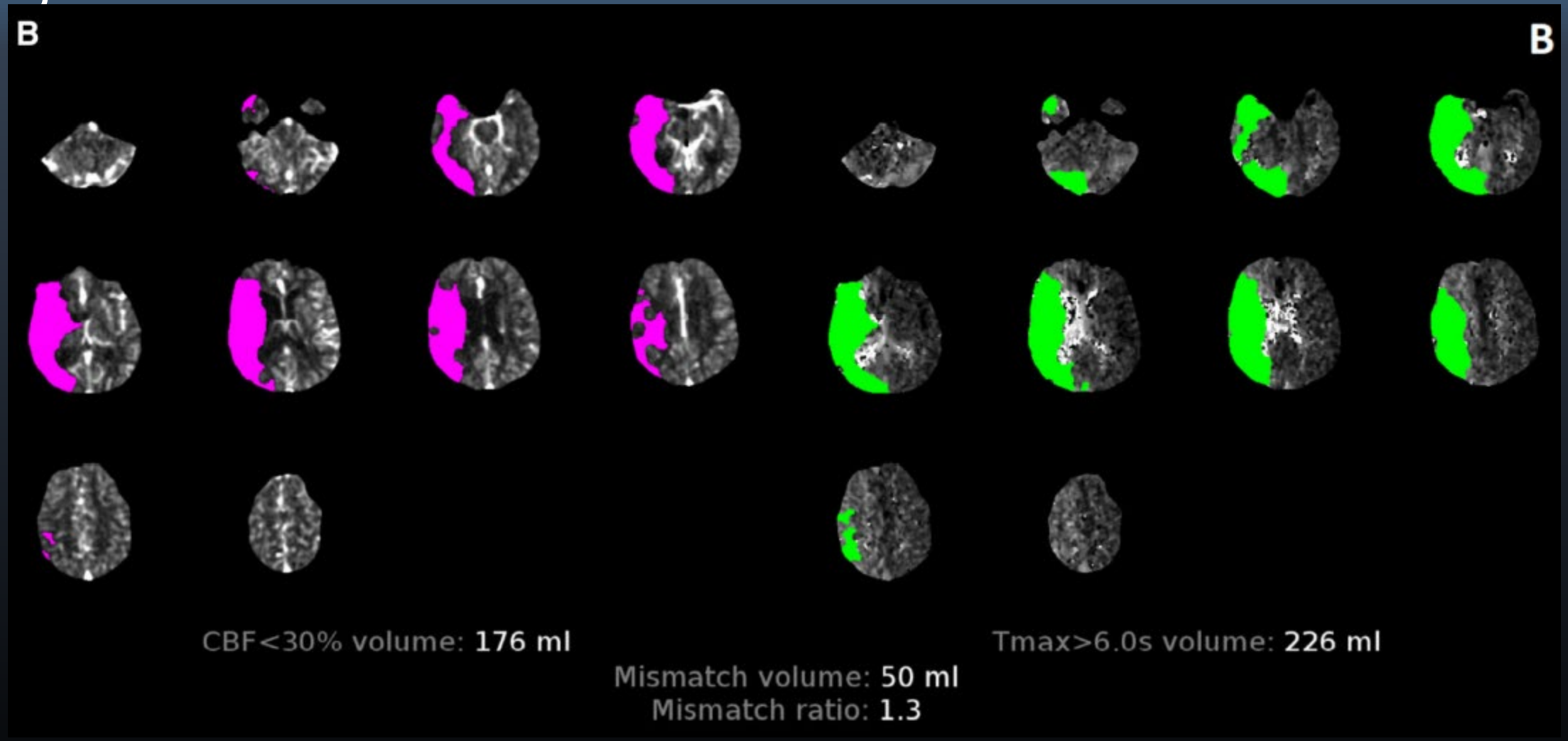
Perfusion Scan Information

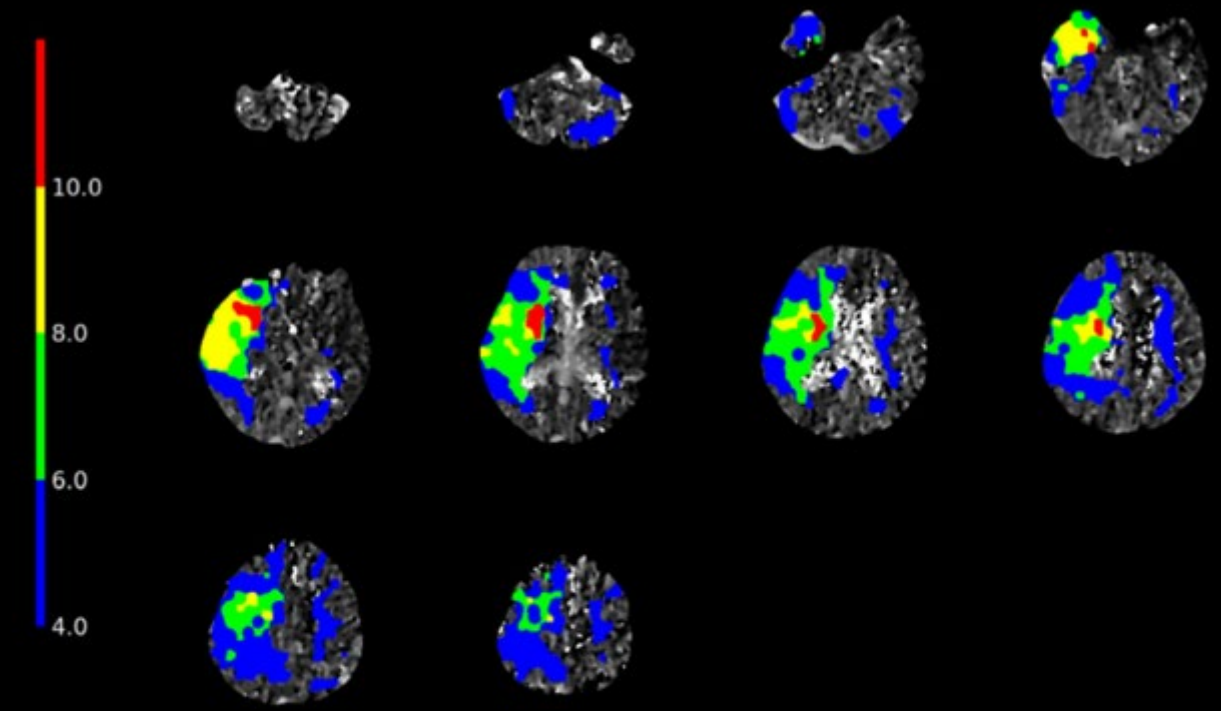
- Identify:
  - Tissue that is likely to infarct in absence of reperfusion
  - Tissue that is already infarcted
- Scan provides both location and amounts of each.
- Core Infarct predicted for tissue with < 30% normal blood volume
  - This may be overestimated with hyper acute stroke and rapid reperfusion
- Salvageable (penumbral) tissue is outside the core but showing late arrival of contrast more than 6 seconds (Tmax >6)

2


A
A
CBF<30% volume: 9 ml
Tmax>6.0s volume: 126 ml
Mismatch volume: 117 ml
Mismatch ratio: 14.0

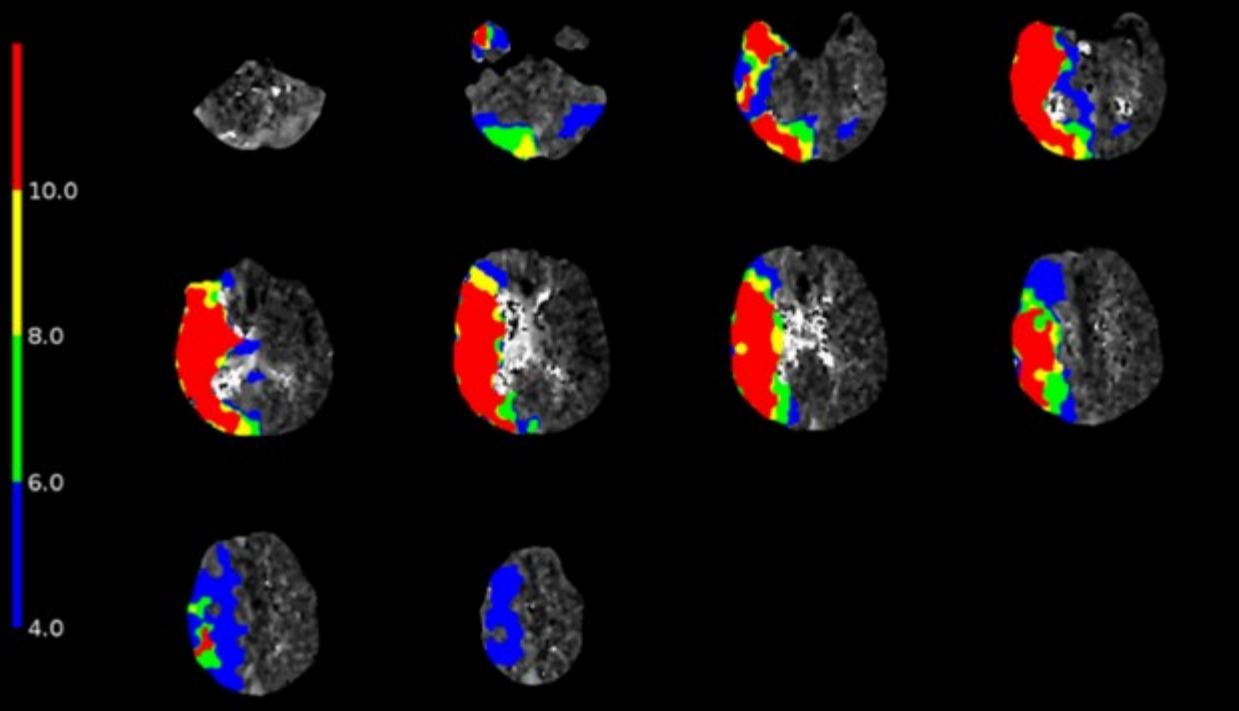
2


B
B
CBF<30% volume: 176 ml
Tmax>6.0s volume: 226 ml
Mismatch volume: 50 ml
Mismatch ratio: 1.3



Tmax>10.0s volume: **9 ml**
Tmax>8.0s volume: **42 ml**
Tmax>6.0s volume: **126 ml**
Tmax>4.0s volume: **322 ml**
Hypoperfusion Index (Tmax>10s/Tmax>6s): 0.1

Large Tmax>4 Slow progression



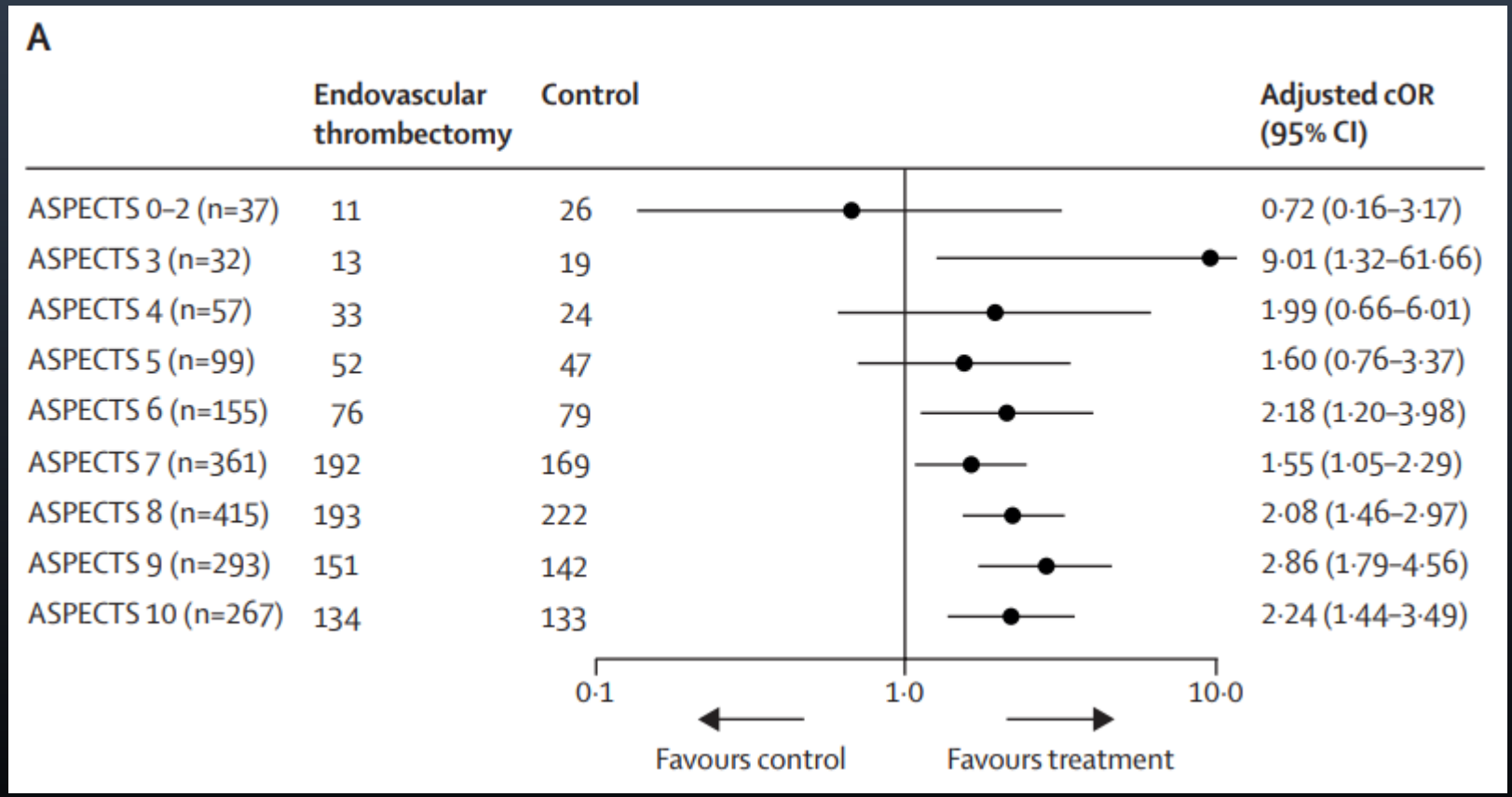
Tmax>10.0s volume: **155 ml**
Tmax>8.0s volume: **184 ml**
Tmax>6.0s volume: **226 ml**
Tmax>4.0s volume: **329 ml**
Hypoperfusion Index (Tmax>10s/Tmax>6s): 0.7

Large Tmax>10 Fast Progression

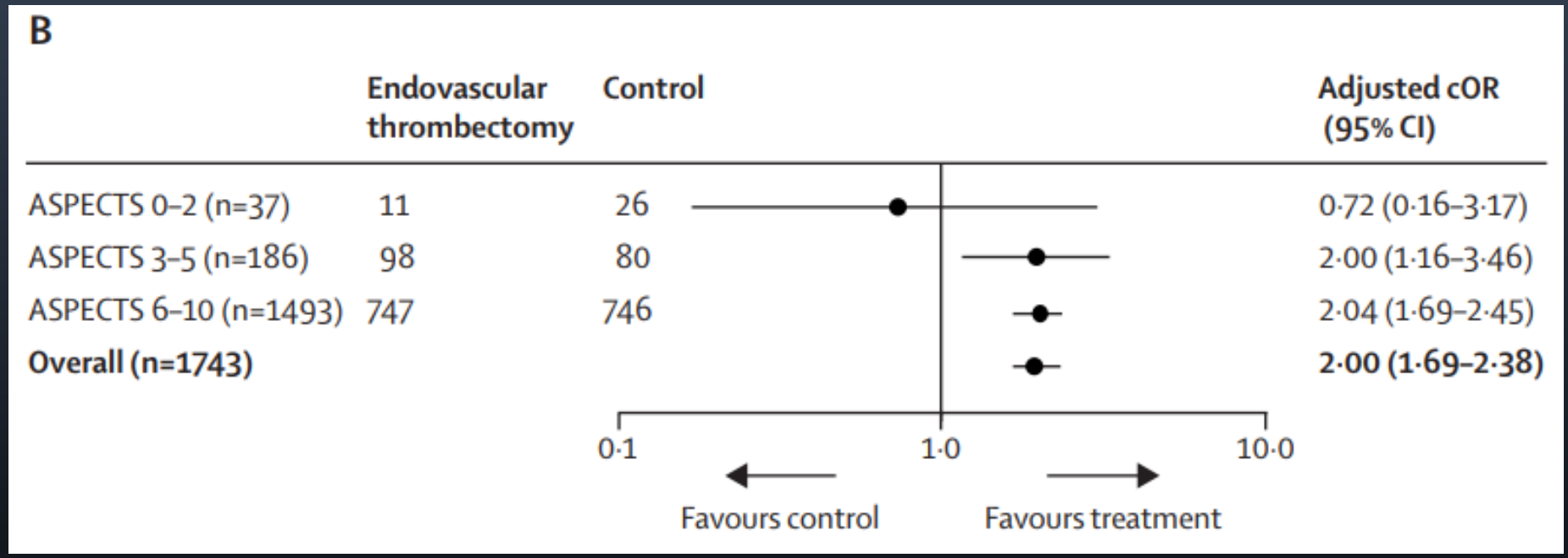
Data from HERMES Collaboration

- Patient level meta-analysis 1764 patients in randomized thrombetomy trials since 2011
- Detailed data on imaging charactoristics including ASPECTS scores
- Patients analyzed thrombectomy versus best medical therapy
- Overall highly significant treatment effect as measured by 90 day disability
  - NNT = 2 (95% CI 1.69-2.38)
- Mortality at 90 days 14.7% vs 17.3% (p=0.15 NS)

ASPECTS Analysis of HERMES Data

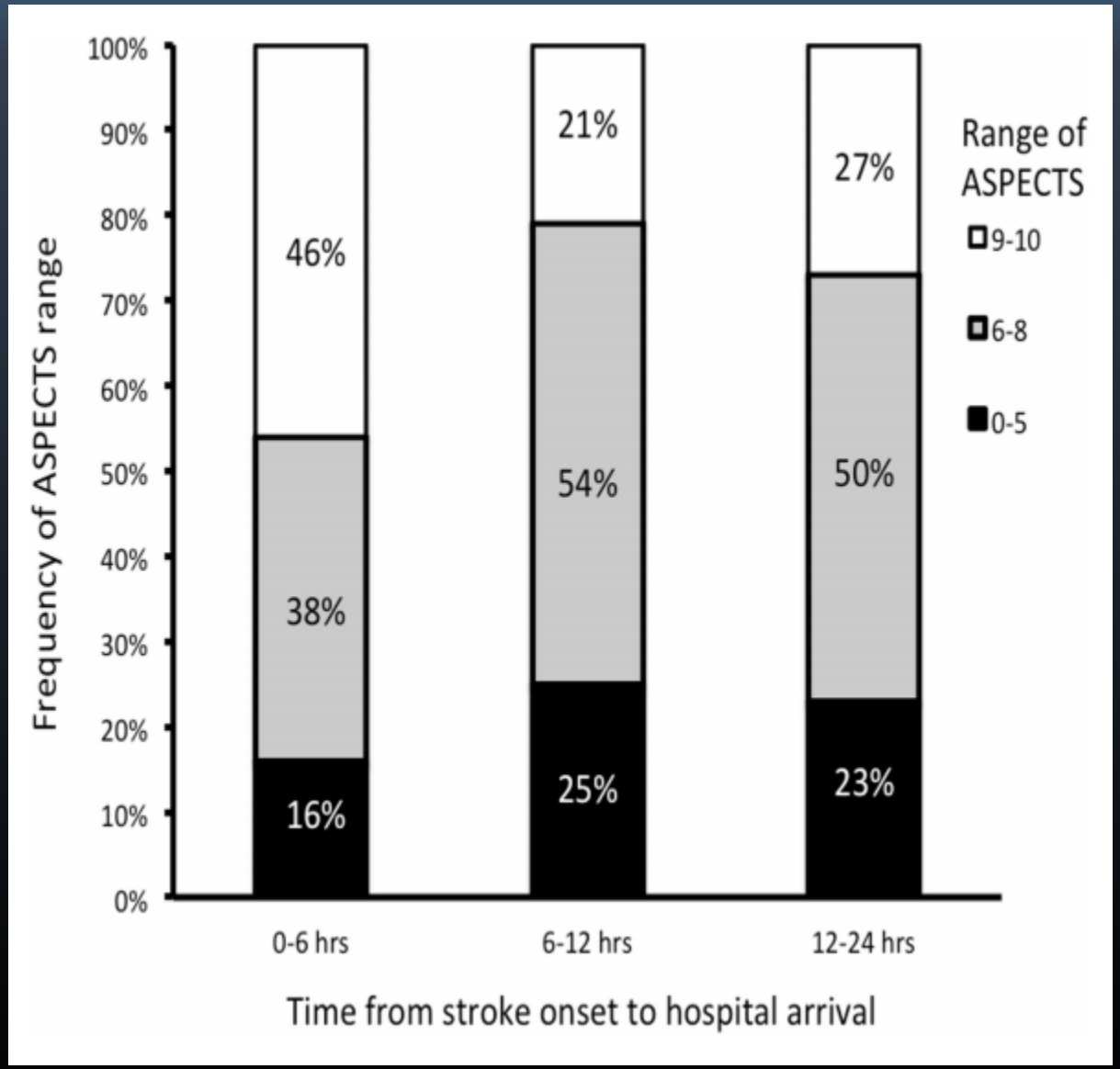


Lancet Neurol 2018; 17: 895–904



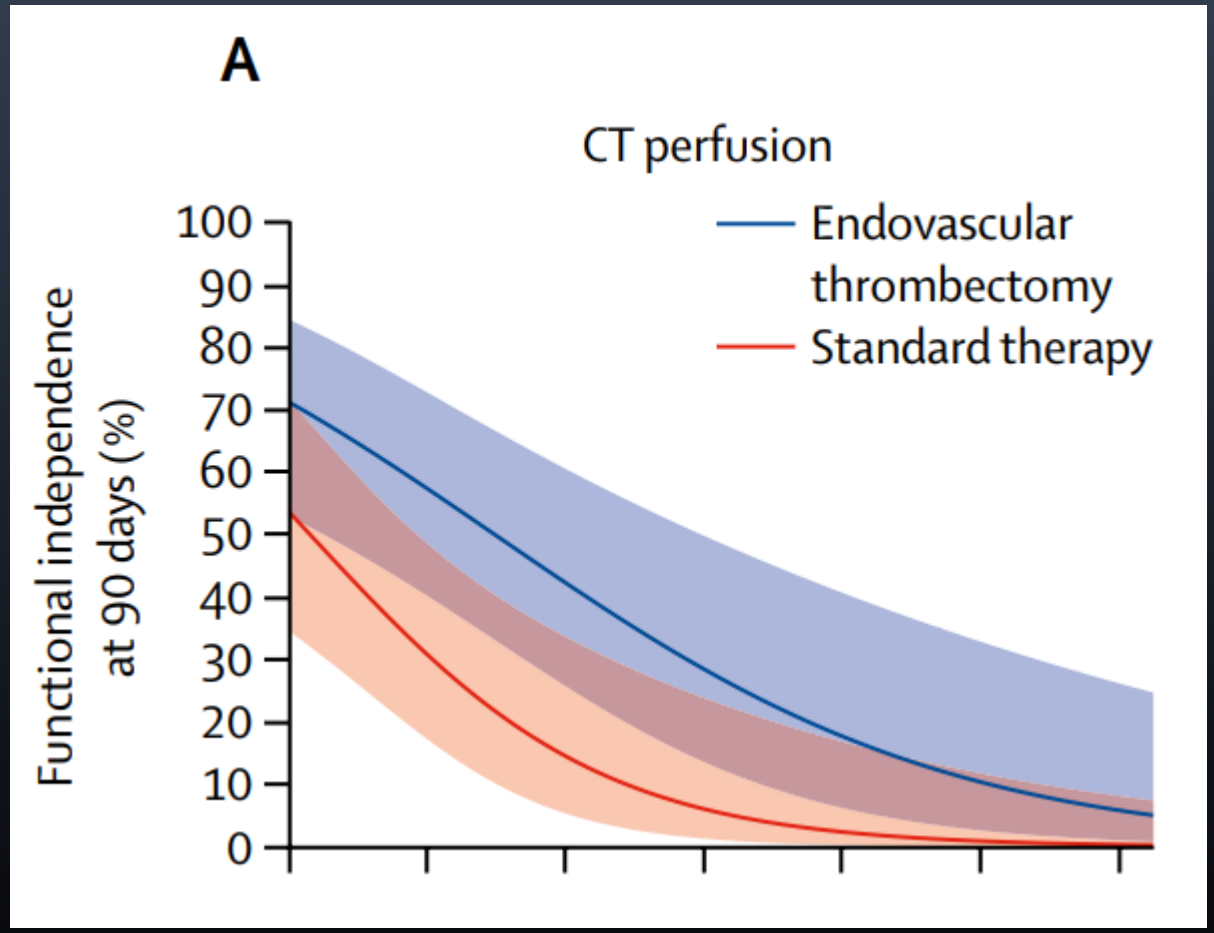
- Hemorrhage in the ASPECTS 0-4 was 19% of 52 treated patients compared to 5% of 66 in medical group. Overall treatment effect with regard to disability was preserved.

198 patients with M1 occlusion presenting at different times



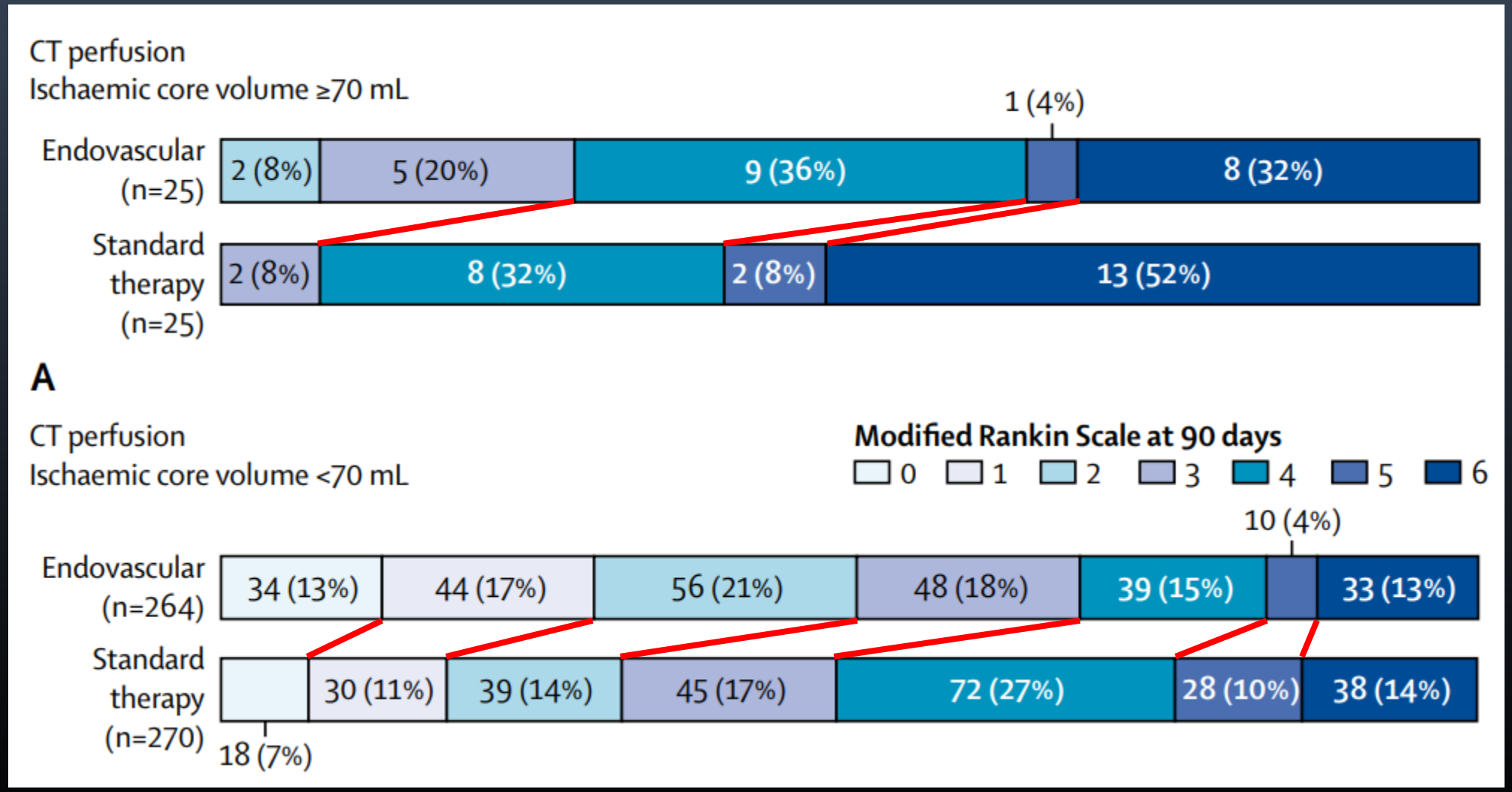
Neurosurgery 83:122–127, 2018

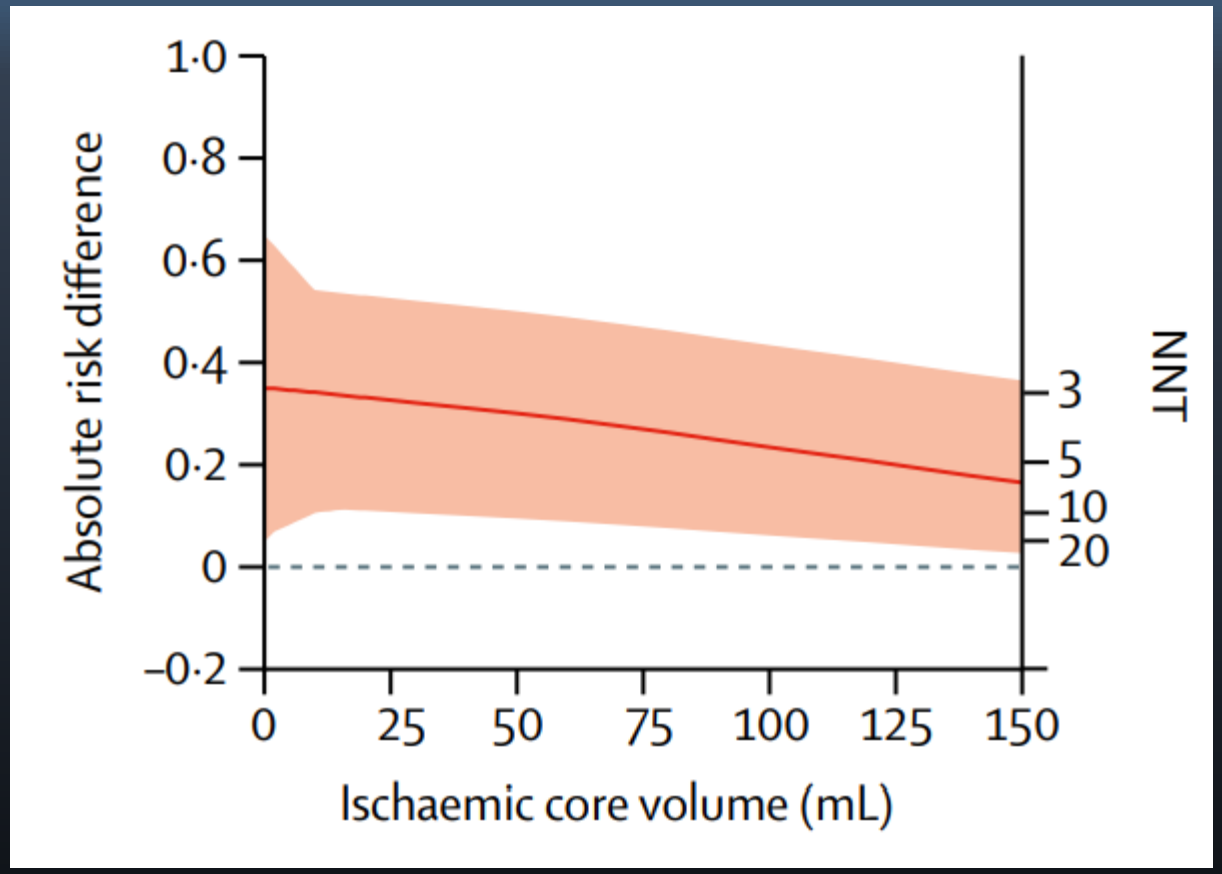
Perfusion Scan Analysis of HERMES Data



Lancet Neurol 2019; 18: 46–55

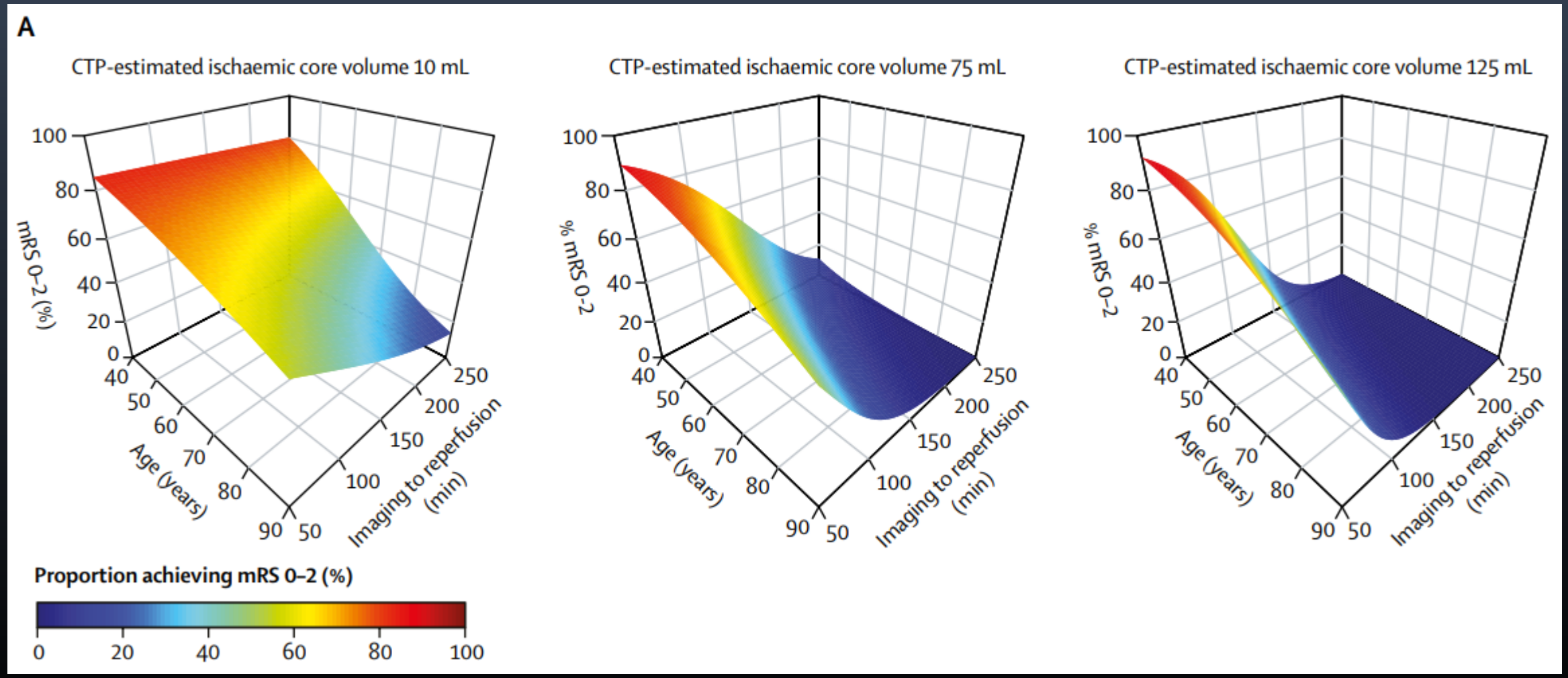
Shift Analysis of Smaller and Larger (> 70 ml) Infarcts





- Core infarct size versus number needed to treat for one category better on disability score

Effect on Disability by Core Size vs Age vs Time



10-mL increase in ischaemic core was approximately equivalent to a 30-min delay to reperfusion or a 5-year increase in age.

Perfusion Scan Lessons

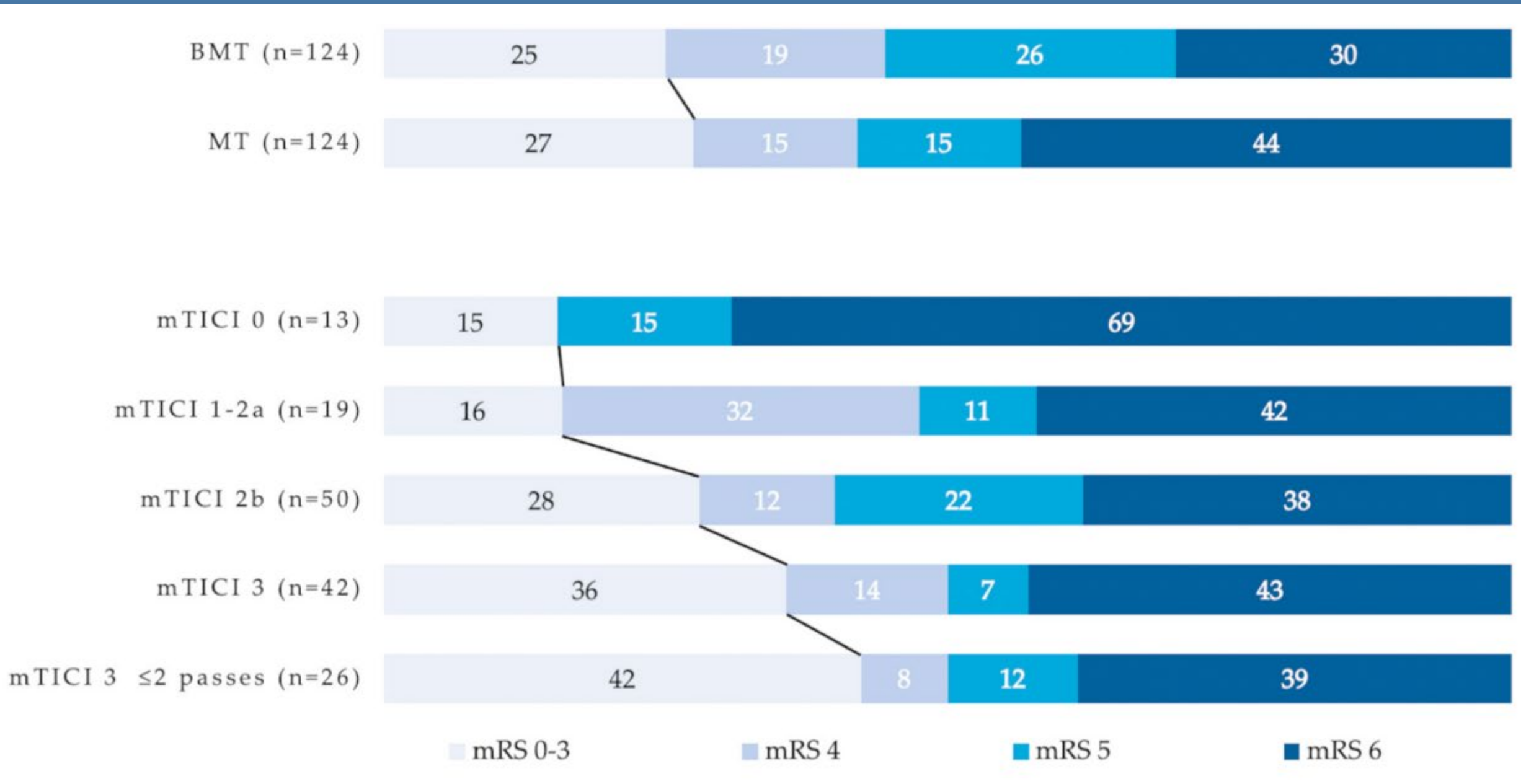
- Core infarct size strongly influences disability
  - Every 10 ml increase in infarct decreases odds of good recovery 20-30%
- But, even large core infarcts benefit from thrombectomy
- Age and time to reperfusion interact with core size to determine disability

Large Core Infarct Intervention

- Arguing for intervening on large core infarcts
  - Natural history of disease is severe disability
  - Thrombectomy candidates may be increased by 35-40%
- Arguing against intervening:
  - May be ineffective procedure
  - May be detrimental due to reperfusion hemorrhage

Natural Experiment

- 248 patients in Germany arriving to 28 hospitals, 3 offering thrombectomy.
- Published as case match control data
- NIHSS 17 in endovascular, NIHSS 19 in best medical therapy
- ASPECTS scores 0-5 (most 4 or 5)
- Good functional outcome in 27.4% of thrombectomy and 25% medical
- Symptomatic hemorrhage 16.1% thrombectomy and 5.6% medical
- Mortality was 43% thromectomy and 29% medical

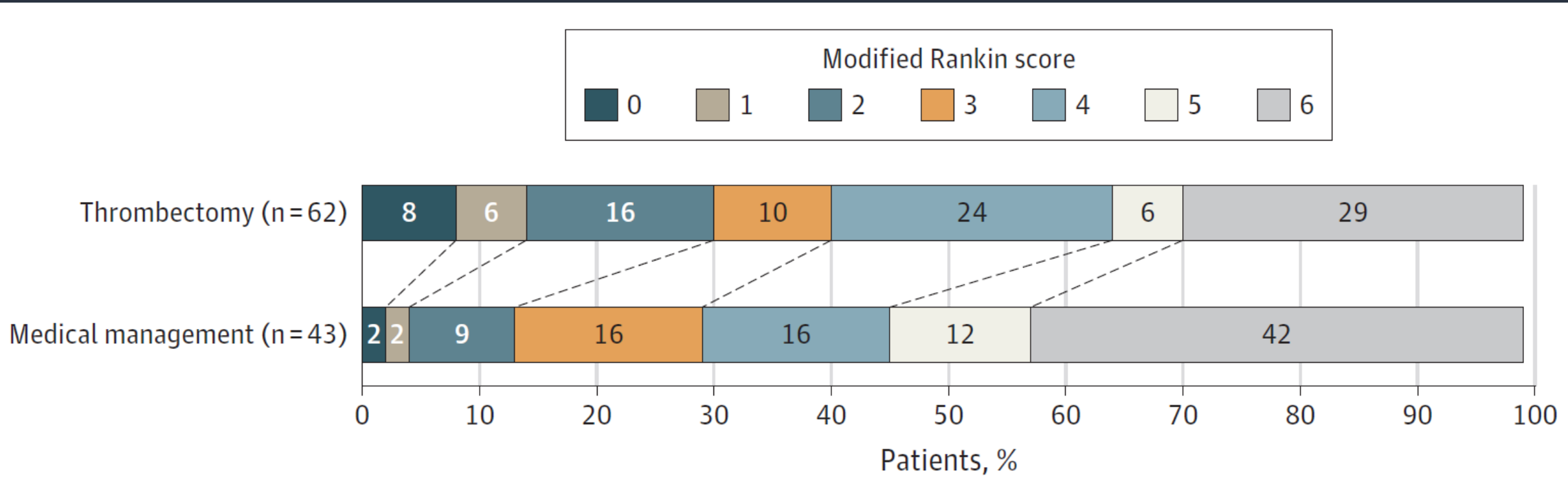

BMT (n=124)
25
19
26
30
MT (n=124)
27
15
15
44
mTICI 0 (n=13)
15
15
69
mTICI 1-2a (n=19)
16
32
11
42
mTICI 2b (n=50)
28
12
22
38
mTICI 3 (n=42)
36
14
7
43
mTICI 3 ≤2 passes (n=26)
42
8
12
39
mRS 0-3
mRS 4
mRS 5
mRS 6

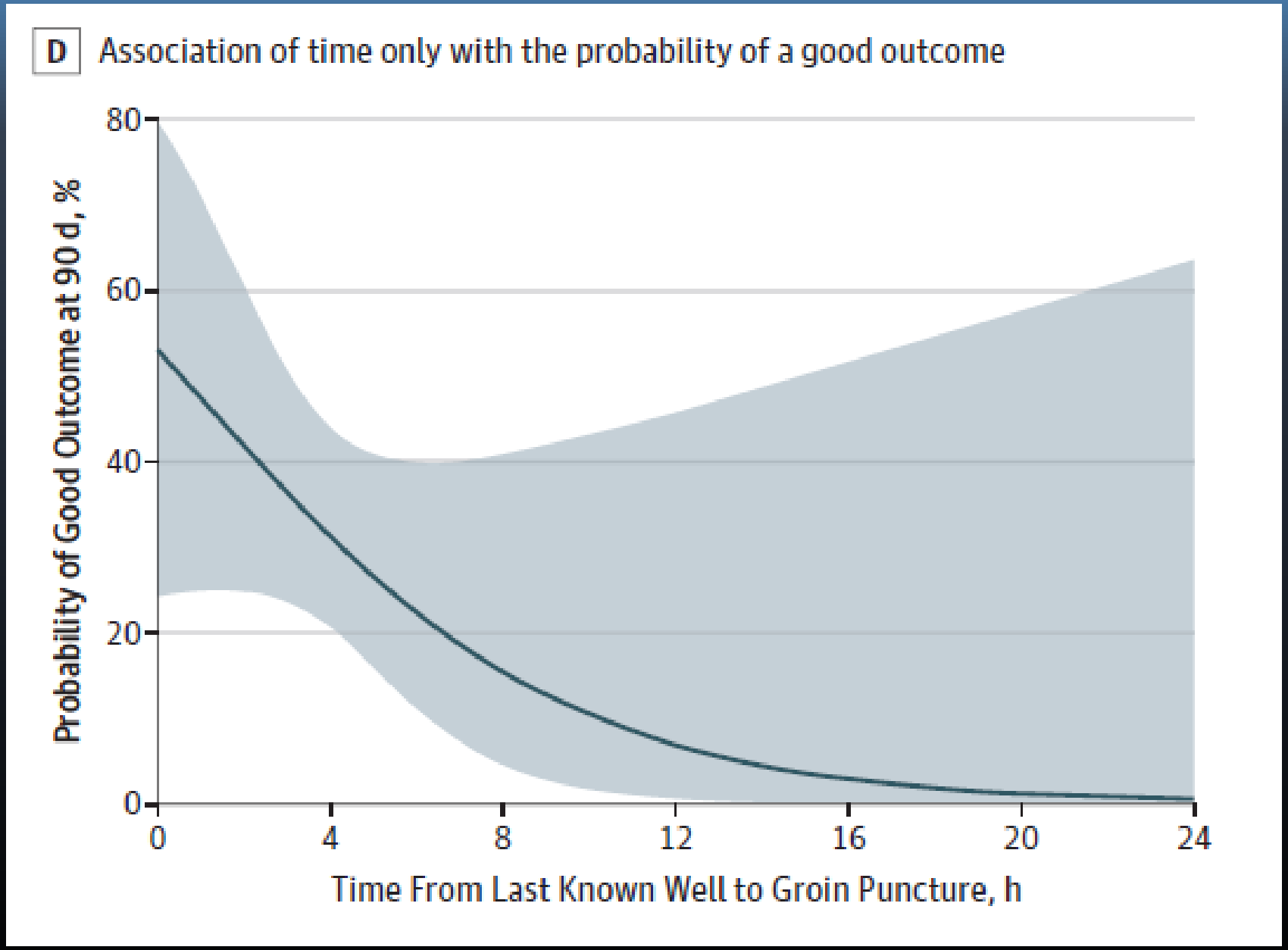
SELECT Trial

- Prospective non-randomized Cohort of patients treated medically or thrombectomy
- ASPECTS 5 or less
- CT Perfusion showing core of more than 50 cm3
- Median mismatch between penumbra and core 120 cm3 for thrombectomy patients and 95 cm3 for medical management patients

JAMA Neurology October 2019 Volume 76, Number 10

Primary Finding




D
Association of time only with the probability of a good outcome
Probability of Good Outcome at 90 d, %
80
60
40
20
0
0
4
8
12
16
20
24
Time From Last Known Well to Groin Puncture, h

Other Outcomes

Characteristic	Thrombectomy	Medical	p
Good to moderate Outcome (mRs 0-3)	40%	30%	0.29
Symptomatic hemorrhage	13%	7%	0.51
Death	29%	42%	0.17
Final Infarct Volume	97 cm3	190 cm3	0.001

Take Home Points

- Large core infarct stroke is a devastating disease
- Data is conflicting as to whether thrombectomy beneficial in these patients
- Age, and time to reperfusion and infarct size play a role in who might benefit
- Randomized control trials needed to establish or refute thrombectomy in these patients
- Possibly results will be bimodal, some made better some worse.

TESLA Trail

- Prospective, Randomized, open-label, blinded endpoint trial
- Occlusion of intracranial ICA and/or MCA M1 segment
- Moderate to large infarcts ASPECTS 2-5
- NIHSS > 6; baseline good functional status (mRS 0 or 1)
- Randomize within 24 hour last known well
- Start case within 60 minutes of CT imaging.

- Patients are randomized to best medical therapy or thrombectomy

Two Questions for the Audience

Which ASPECTS score is better for the patient?

A) Ten

B) Zero

Which ASPECTS score is better for the patient?

A) Ten

B) Zero

Rank the importance of predictors of stroke recovery in thrombectomy patients:

A) Time to reperfusion > patient age > core infarct size
B) Core infarct size > patient age > time to reperfusion
C) Patient age > time to reperfusion > core infarct size
D) Time to reperfusion > core infarct size > patient age

Rank the importance of predictors of stroke recovery in thrombectomy patients:

A) Time to reperfusion > patient age > core infarct size

B) Core infarct size > patient age > time to reperfusion

C) Patient age > time to reperfusion > core infarct size

D) Time to reperfusion > core infarct size > patient age