Clinical update no. 511
28 March 2018

Recent stroke thrombectomy trials have provided evidence that has already made its way into the Guidelines. What's new?

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

Stroke March 2018 http://stroke.ahajournals.org/content/49/3/e46

3.7. Mechanical Thrombectomy

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1. Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered.	I
2. In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	III: Harm
3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.	I

At least the above is in line with the evidence: prestroke mRS 0-1 (functionally independent), ICA or proximal MCA occlusion, NIHSS ≥6, groin puncture within 6hr of symptom onset.

4. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for

The Guideline goes on to acknowledge a lack of evidence for thrombectomy in other stroke types, but where it "*may be reasonable*; i.e. more distal MCA occlusion, anterior cerebral, vertebral, basilar artery, or posterior cerebral arteries. Also prestroke mRS >1 and milder stroke with NIHSS <6.

Additional randomized trial data are needed.

No good evidence, but do it anyway.

7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I
8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa

Two trials, DAWN and DEFUSE 3, showed benefit in selected patient beyond 6 hours.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

for the DEFUSE 3 Investigators*

N ENGL J MED 378;8 NEJM.ORG FEBRUARY 22, 2018

182 patients were randomised. Inclusion criteria were proximal MCA or internal carotid artery occlusion; initial infarct size < 70 ml; and a ratio of ischaemic/infarct volume > 1.8. Thrombectomy + standard care was compared to standard care alone. IV t-PA was allowed if given within 4.5 hours of onset (given in about 10% in each group). Primary outcome was mRS at 90 days. The trial was terminated early for efficacy.

There was an mRS of 0-2 (functionally independent) in 45% with thrombectomy v 17% for standard care, P<0.001, and reduced mortality at 90 days of 14 v 26%, p = 0.05. Symptomatic ICH in 7 v 4%, P = 0.75.

CONCLUSIONS

Endovascular thrombectomy for ischemic stroke 6 to 16 hours after a patient was last known to be well plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion and a region of tissue that was ischemic but not yet infarcted. (Funded by the National Institute of Neurological Disorders and Stroke; DEFUSE 3 ClinicalTrials.gov number, NCT02586415.)

Table 1. Baseline Characteristics of the Patients and Features of Thrombectomy.*

Characteristic	Endovascular Therapy (N=92)	Medical Therapy (N=90)
	No./%	
NIHSS score	16 (10–20)	16 (12–21)
t-PA given	10 (11)	8 (9)
Ischaemic core (ml)	9.4 (2.3–25.6)	10.1 (2.1–24.3)
Perfusion lesion (ml)	114.7 (79.3–146.3)	116.1 (73.4–158.2)

Table 2. Clinical and Imaging Outcomes.

Characteristic	Endovascular Therapy (N=92)	Medical Therapy (N=90)
	No./%	
Symptomatic ICH	6 (7)	4 (4)
Infarct vol at 24hr (ml; median)	35 (18–82)	41 (25–106)
		P = 0.19
Infarct growth at 24hr (ml)	23 (10–75)	33 (18–75)
		P = 0.08
Reperfusion >90% (24hr)	59/75 (79)	12/67 (18)
		P < 0.001
Complete recanalisation (24hr)	65/83 (78)	14/77 (18)
		P < 0.001

Available at http://www.heti.nsw.gov.au/programs/emergency-medicine-training/emergency-medicine-training-test/educational-resources/em-clinical-updates/

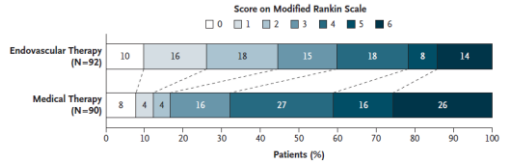

Figure 2. Scores on the Modified Rankin Scale at 90 Days.

mRS: 0 no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, 6 death

DISCUSSION

Despite clinical benefit with thrombectomy, between-group differences in 24-hour infarct volume and growth after thrombectomy were not significant.

Somewhat curious that despite reperfusion and improved functional outcome there was no significant effect on infarct volume. There is clearly more to stroke recovery than reperfusion and infarct size.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

for the DAWN Trial Investigators*

January 4, 2018
N Engl J Med 2018; 378:11-21

NEJM QuickTake www.nejm.org/doi/full/10.1056/NEJMoa1706442 Manufacturer sponsored; list of conflicts (compressed to fit).

The DAWN trial enrolled patients based on a mismatch of clinical stroke severity and infarct volume seen on CT at presentation, with ICA or proximal MCA occlusion.

Enrolment was stopped early for efficacy, with 206 patients enrolled. There was functional independence at 90 days in 49% with thrombectomy v 13%. Mortality (18%) and symptomatic ICH (6 v 3%) were not statistically different (study funded by Stryker Neurovascular).

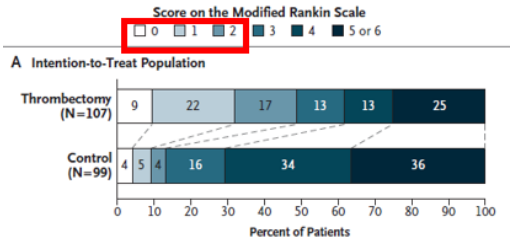

Table 2. Efficacy Outcomes.*

Outcome	Thrombectomy Group (N=107)	Control Group (N=99)	Absolute Difference (95% CI)†
Recanalization at 24 hr — no. (%)††	82 (77)	39 (39)	40 (27–52)
Change from baseline in infarct volume at 24 hr — ml††			
Median	1	13	
Interquartile range	0–28	0–42	
Infarct volume at 24 hour — ml††			
Median	8	22	

Unlike DEFUSE 3 the better reperfusion was associated with smaller infarct volume.

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

Key new recommendations are:

Expanded Time Window for Mechanical Thrombectomy: based on the above trials. Strict compliance with inclusion criteria used in the trials is recommended (at least for now)

Vascular Imaging: perform vascular imaging during the initial imaging; don't delay for creatinine level if no history renal impairment. Imaging should not delay t-PA if indicated.

Perfusion Imaging: CT or MRI perfusion or diffusion-weighted-MRI is recommended if considering thrombectomy beyond 6hr to ensure strict compliance with inclusion criteria of DAWN and DEFUSE-3 trials.

Routine Diagnostic Testing: The following testing is of no benefit and is not recommended: routine cholesterol testing, sleep apnoea screening, routine brain MRI, routine intracranial CTA or MRA (unless used to guide acute intervention), echocardiography, and MRI to exclude cerebral micro bleeds before IV alteplase.

Ensuring patient access to intervention requires effective systems of care.

The Guideline contains a lot more, including the evolving inclusion criteria and contraindications to thrombolysis.

Available at http://www.heti.nsw.gov.au/programs/emergency-medicine-training/emergency-medicine-training-test/educational-resources/em-clinical-updates/