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

NEJM Quicktake: https://www.nejm.org/do/10.1056/NEJMdo005240/full/

Clinical question:
Among patients with acute stroke between 6-24 hours of symptom onset, does thrombectomy improve 90-day outcomes compared to standard care alone?

Background:
Endovascular thrombectomy had been proven superior to standard care alone among patients with acute stroke when performed within 6 hours of onset in several studies (including the MR CLEAN trial from last week). From these studes it was seen that the benefit of intervention declined as time since onset increased. However, a subset of acute stroke patients have brain tissue that is ischemic but not yet infarcted; these patients have a clinical deficit that is disproportionately severe when compared to the amount of infarcted tissue on imaging. Among these patients, there is limited evidence whether the ischemic tissue may be salvageable with reperfusion through thrombectomy. Therefore, the authors of this trial set out to recruit patients with a mismatch between their clinical deficit and the volume of infarct on imaging studies.

Methods:
Multicenter, prospective, randomized trial with blinded assessment of endpoints. 206 subjects with acute stroke and clinic deficit out of proportion to infarct volume (107: Thrombectomy vs 99: Standard care). Setting: 26 centers in the US, Canada, Europe, and Australia. Enrollment: 2014-2017. Primary outcome: Mean score for disability on the utility weighted modified Rankin scale and the rate of functional independence (a score of 0-2 on the modified Rankin scale) at 90 days. Funding: Stryker Neurovascular

Inclusion criteria:
Acute stroke and persistent occlusion after IV thrombolysis or contraindication to thrombolysis. Age ≥18. Baseline NIHSS ≥10. Randomization occurs between with 6 to 24 hours after time last known well. Pre-stroke modified Rankin score <2. Anticipated life expectancy ≥6 months. <1/3 MCA territory involved as assessed by CT or MRI. Occlusion of either intracranial ICA and/or M1 via MRA or CTA

Clinical Imaging Mismatch (CIM) via MR-DWI or CTP-rCBF:

- 0 - 20 core infarct, NIHSS ≥ 10, age ≥ 80 years
- 0 - 30 cc core infarct, NIHSS ≥ 10, age < 80 years
- 31 - 50 cc core infarct, NIHSS ≥ 20, age < 80 years

Exclusion criteria:
Severe head injury within 90 days. Rapid improvement to NIHSS <10 or vessel recanalization prior to randomization. Pre-existing neurological or psychiatric disease. Seizures at stroke onset. Blood glucose <50mg/dL or >400mg/dL. Hemoglobin <7 mmol/L. Platelets <50,000/uL. Sodium <130 mmol/L, potassium <3 mEq/L or >6 mEq/L. Renal failure. Hemorrhagic diathesis or INR >3.0 or PTT >3 times normal. Active or recent hemorrhage within 30 days. Severe allergy to contrast medium. Systolic Blood Pressure >185 mmHg or Diastolic Blood Pressure >110 mmHg. Pregnancy or lactation. Participation in another study. Presumed septic embolus or suspicion of bacterial endocarditis. Prior treatment with thrombectomy intra-arterial therapies. Intracranial hemorrhage. Flow limiting carotid dissection, high-grade stenosis, or

complete cervical carotid occlusion. Excessive cervical vessel tortuosity. Suspected cerebral vasculitis. Suspected aortic dissection. Existing stent in the same vascular territory. Occlusions in different vascular territories. Significant mass effect/midline shift. Intracranial tumor

Results:

The primary end point of the mean score for disability on the utility-weighted modified Rankin scale at 90 days was 5.5 in the thrombectomy group as compared with 3.4 in the control group (adjusted difference: 2.0 points, confidence interval: 1.1 to 3.0, posterior probability of superiority >.999). The secondary primary end point of the rate of the functional independence (a score of 0, 1, or 2 on the modified Rankin scale) at 90 days was 49% in the thrombectomy group and 13% in the control group (adjusted difference: 36 points, 95% confidence interval: 21 to 44, posterior probability of superiority >.999). The rates of safety endpoints and serious adverse events (including stroke-related death at 90 days, death from any cause at 90 days, and symptomatic intracerebral hemorrhage) did not differ significantly between treatment groups

Conclusions:

In patients with intracranial internal carotid artery or proximal MCA strokes who had mismatch of clinical symptoms vs infarct volumes and who were last seen 6-24 hours prior, thrombectomy is superior with regard to functional independence and disability at 90 days.

Additional study of interest:

On September 9th, 2021 NEJM released the first observational multicenter trial evaluating movile stroke units and how much they alter outcomes vs standard EMS units.

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