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Emergency Department Selection of Acute Ischemic Stroke Patients for Potential Endovascular Reperfusion Therapy

Why is this topic important? The emergency physician plays a critical role in the rapid identification of stroke syndrome and initiation of appropriate imaging, consultations, and interventions. Recent research has demonstrated a large magnitude of beneficial effects for mechanical thrombectomy in select patients with acute ischemic stroke (AIS), but the benefits are time limited. (1-3)

How will this change my clinical practice? Advanced imaging is required to determine which patients are candidates for mechanical thrombectomy, i.e., endovascular reperfusion therapy. In consultation with the stroke neurologist or neuro-interventionalist, emergency physicians facilitate timely intervention by either arranging for rapid transportation to a comprehensive stroke center or by ordering appropriate advanced imaging studies if readily available in their emergency department (ED). (1) The time window for mechanical thrombectomy has recently been extended up to 24 hours from last known normal for select patients with salvageable brain tissue along with other specified criteria.

Synopsis Focus Points:

- **Emergency physicians should evaluate every acute (<24 hours since symptom onset) stroke patient as a potential candidate for mechanical thrombectomy.**
- **Randomized trials have shown that the patients most likely to benefit from mechanical thrombectomy have a National Institutes of Health Stroke Scale (NIHSS) ≥ 6, evidence of a large anterior circulation vessel occlusion with salvageable brain tissue on advanced imaging, and are functionally independent at baseline (e.g., mRS 0-2).**

Background:

The American Heart Association Stroke Council 2019 update to their AIS guidelines include strong recommendations (Class I) based on high-quality evidence (Level A) that are directly relevant to the ED selection of patients suspected of AIS that may be candidates for mechanical thrombectomy. (1) A few of the key points are paraphrased here:

- Advanced imaging, CT, or MR angiography should be obtained as quickly as feasible.

- Criteria for mechanical thrombectomy –

    - within 6 hours of symptom onset:
        - Adults with pre-stroke Modified Rankin Scale (mRS) disability of 0 to 1
        - Causative large vessel occlusion (LVO) of the internal carotid artery or middle cerebral artery segment 1
        - NIHSS score of ≥ 6**
        - Alberta Stroke Program Early CT Score (ASPECTS) of ≥ 6

    - within 6 to 16 hours of last known normal: who have anterior circulation LVO should be based on DAWN or DEFUSE 3 eligibility criteria. (4,5)
    - within 16 to 24 hours of last known normal: who have anterior circulation LVO should be based on DAWN eligibility criteria. (4)

Summary of DAWN inclusion criteria prior to advanced CT or MR angiography: (4)

1. Adult with NIHSS ≥ 10**
2. Disability mRS ≤ 1 prior to acute stroke
3. No evidence of intracerebral hemorrhage on CT or MRI
4. No evidence of infarct involving > ⅓ middle cerebral artery territory

Summary of DEFUSE 3 clinical inclusion criteria prior to advanced CT or MR angiography: (5)

1. Adult with NIHSS ≥ 6**
2. Disability mRS ≤ 2 prior to acute stroke (functionally independent for all ADLs)
3. Endovascular treatment can be initiated (femoral puncture) between 6 and 16 hours of stroke onset (stroke onset defined as the time last known to be at neurologic baseline)

Benefits in 90-day functional outcomes were seen in both DAWN and DEFUSE 3. (4,5) For the DAWN trial, 49% of the thrombectomy group had mRS score 0 to 2 at 90 days compared to 13% in the control arm; adjusted difference, 33% (95% CI: 21 to 44). For DEFUSE 3, 45% in the thrombectomy group had mRS score 0 to 2 at 90 days compared to 17% in the control; OR = 2.7 (95% CI: 1.6 to 4.5). (4, 5) There was no significant difference in the rates of symptomatic intracerebral hemorrhage in either study. A systematic review published in 2020, showed endovascular treatment is superior to general treatment for acute ischemic stroke patients with age < 70, NIHSS ≥ 20 and maximum delay for intervention is 5 hours. (6)

This is Level 1a evidence. (7)

**The Society of NeuroInterventional Surgery Guidelines state “Thrombectomy may be considered in patients with anterior circulation AIS and NIHSS <6 when associated with disabling symptoms (class IIa, level B-NR)." (8)

Table: Selection of patients with **anterior circulation LVO** for potential mechanical thrombectomy based on AIS (1), DAWN (4), and DEFFUSE 3 (5) criteria.

Reference	Last Known Well	CT or MRI Findings	Key Inclusion Criteria	Key Exclusion Criteria
AIS guideline[1]	**< 6 hours**	ASPECT score ≥ 6; CTA or MRA is recommended but the utility of additional advanced imaging such as perfusion and diffusion imaging is unclear	Adults ≥ 18 years with **NIHSS ≥ 6** and baseline mRS 0-1	Standard alteplase exclusions
DEFUSE 3[5]	**6 to 16 hours**	Core mismatch ratio > 1.8, mismatch volume > 15 mL, and ischemic core volume < 70 mL; ASPECT score ≥ 6; no mass effect; multiple territory infarcts	Adults 18-90 years with **NIHSS ≥ 6** but ≤ 25, and baseline mRS 0-2	Standard alteplase exclusions including BP > 185/110; terminal illness with life expectancy < 6 mo; taking anticoagulant; Hx diabetes and prior stroke; seizure resulting in inability to obtain accurate NIHSS
DAWN[4]	**6 to 24 hours**	Clinical-core mismatch according to age and imaging results; no evidence of infarct involving 1/3 of middle cerebral artery	Adults ≥ 18 years with **NIHSS ≥ 10** and baseline mRS 0-1	Standard alteplase exclusions including BP > 185/110

References:

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2. Jahan R, Saver JL, Schwamm LH, et al. Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA*.2019; 322 (3):252-263. doi:10.1001/jama.2019.8286

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4. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, et al. DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mis-match between deficit and infarct. *N Engl J Med.* 2018; 378:11–21. doi: 10.1056/NEJMoa1706442

5. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, et al. DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med.* 2018; 378:708–718. doi: 10.1056/NEJMoa1713973

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7. https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

8. Mokin M, Ansari SA, McTaggart RA, Bulsara KR, Goyal M, Chen M, Fraser JF; Society of NeuroInterventional Surgery. Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO): report of the SNIS Standards and Guidelines Committee. J Neurointerv Surg. 2019 Mar;11(3):215-220. doi: 10.1136/neurintsurg-2018-014640.

Resources for additional learning:

NIHSS Stroke Score Calculator: https://www.mdcalc.com/nih-stroke-scale-score-nihss

Modified Rankin Scale (disability) Calculator: https://www.mdcalc.com/modified-rankin-scale-neurologic-disability

Alberta Stroke Program Early CT Score (ASPECTS: https://www.mdcalc.com/alberta-stroke-program-early-ct-score-aspects

https://pubmed.ncbi.nlm.nih.gov/?term=acute%20ischemic%20stroke%20therapy&pos=1

https://emergencymedicinecases.com/?s=stroke

http://thesgem.com/2020/05/sgem292-with-or-without-you-endovascular-treatment-with-or-without-tpa-for-large-vessel-occlusions/

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