

## EVMS JC: Critical Appraisal Worksheet: Systematic Review/Meta-analysis

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**Citation:**

Jovin, T. G. et al., Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (Aurora): A systematic review and individual patient data meta-analysis. *The Lancet*, 399(10321), 249–258. [https://doi.org/10.1016/s0140-6736\(21\)01341-6](https://doi.org/10.1016/s0140-6736(21)01341-6)

<b>Guide</b>	
1. Did the review explicitly address a sensible question?	The review addressed the role of thrombectomy intervention in patients with salvageable brain tissue in the setting of anterior circulation stroke from 6 hours and up to 24 hours.
2. Was the search for relevant studies details and exhaustive?	Uncertain. Search terms were limited to 6 items “Stroke, endovascular, large vessel occlusion, and 6 hours” searching from 1/1/2000-3/1/2021 and included only RCT’s. These were then assessed for trials that included thrombectomy intervention plus standard medical treatment verses standard medical treatment alone for those patients presenting with greater than 6 hours since symptom onset in ischemic stroke. No language exclusion. No kappa score reported on articles to include,
3. Were the primary studies of high methodological quality?	Probably. The authors did not use the broadly accepted <a href="#">PRISMA</a> criteria for developing a systematic review. That stated, All 6 were RCT’s. 3 studies included <26 participants which raise questions of their impact as individual studies. Four of the 6 studies were stopped early and did not meet their predetermined <a href="#">sample size requirements</a>
4. Were the criteria for study inclusion pre-determined and clearly stated?	Yes, RCT’s that included patient’s with anterior circulation ischemic strokes with onset greater than 6 hours that received 2 <sup>nd</sup> generation thrombectomy plus standard medical care verses those that only received standard medical care. No studies were excluded that met inclusion criteria. Medical care generally excluded thrombolytics as all patients were likely beyond the treatment window at the time of the respective studies.
5. Did the authors adequately assess the quality of the included studies?	They limited the studies to only published RCT’s. Two studies represented a majority of the patients included. Further analysis of the studies is difficult to determine; although it is noted 4/6 studies were stopped early and there is concern for overestimation of treatment effect and as previously noted 3-4 of the studies were likely

	underpowered.
<b>CLINICAL IMPORTANCE</b>	
6. What were the overall results of the review?	<p>Overall results of the review showed benefits of thrombectomy for patients 6-24 hours since symptom onset in large vessel occlusion anterior circulation stroke.</p> <p><b>Primary Outcome</b> mRs (0-2) 90Days Favors Intervention : Adjusted OR of 2.54 (95% CI 1.83–3.54) Unadjusted OR 2.42 (95% CI 1.76-3.33) NNT=3</p> <p><b>Safety Outcomes:</b> <b>90D mortality</b> no difference adjusted OR 0.96 [95% CI 0.58–1.60] (crosses 1)</p> <p><b>Intracranial hemorrhage</b> no difference OR 1.74 [0.70–4.31] (crosses 1 wide CI 4.31 could be problematic.</p>
8. Were the results similar from study to study?	The authors note “no heterogeneity in “treatment results” but the authors did report <a href="#">heterogeneity</a> or the I <sup>2</sup> statistic that reports on differences in methodology which when high (>.60) is problematic. Two studies for example did not use perfusion scanning but were included in cohort.
<b>APPLICABILITY</b>	
9. How can I best interpret the results to apply them to the care of my patients?	Broad study population from North America, Europe and Asia. These results should be applied by broadening our inclusion criteria of patients that may benefit from thrombectomy to up to 24 hours since symptom onset. Certainly can help inform patient-centered decision making.
10. Were all patient important outcomes considered?	Yes. Patient centered outcomes were included such at the modified Rankin Scale at 90 days, NIHSS at 24 hours, and early neurologic recovery at 24 hours, mortality at 90 days, and symptomatic intracerebral hemorrhage. Important notes were a NNT of 3 for decreased disability in the thrombectomy group and of these 81% achieved functional independence. There was no statistical difference in cerebral hemorrhage between the groups; however, the studies were likely underpowered as evidenced by the wide CI's for ICH. (0.70-4.31). There were an increased number of symptomatic cerebral hemorrhages in the intervention group. I do believe better mRS scores @ 90D is an important patient centered outcome.
	Strokes are a leading cause of morbidity and

<p>11. Are the benefits worth the costs and potential risks?</p>	<p>mortality in the United States. With a NNT of 3 for Yes. Decreased disability, including a large amount that achieve functional independence, status post thrombectomy compared to medical therapy alone. The cost to persons and likely society is improved with intervention. Further studies should work to address concern for possible increased symptomatic cerebral hemorrhages in the intervention group.</p>
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**Limitations:**

- Focused on hospitals that are comprehensive stroke centers may not be applicable to community setting or less experienced interventionalists.
- Small studies none of which reached their initial sample size requirements. Did not really report on quality parameters of individual studies required in PRISMA guidelines.
- Patient populations presenting greater than 24 hours, those with NIHSS < 6, those with prior mRS >2, and those with posterior circulation strokes cannot be included.
- There is also the overestimation concern as 4/6 studies were stopped early.
- All authors have major financial interests (stocks, options, direct compensation etc) in companies representing thrombectomy devices.

**Clinical Bottom Line:** Patients who present to the emergency department up to 24 hours after symptom onset with anterior circulation strokes and diagnostic evidence of reversible ischemia based upon perfusion scanning should have a rapid neurointerventional consult for possible thrombectomy.