

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

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Citation: Puzio, T. J., Murphy, P. B., Kregel, H. R., Ellis, R. C., Holder, T., Wandling, M. W., Wade, C. E., Kao, L. S., McNutt, M. K., & Harvin, J. A. (2021). Delayed intracranial hemorrhage after blunt head trauma while on direct oral anticoagulant: Systematic Review and meta-analysis. *Journal of the American College of Surgeons*, 232(6). <https://doi.org/10.1016/j.jamcollsurg.2021.02.016>

Guide	
1. Did the review explicitly address a sensible question?	Yes, with the increasing rates of patients on anticoagulation, it is important to know if observation plus or minus repeat head CT imaging is required in these patients after blunt head trauma to assess for delayed intracranial hemorrhage. The review had a clear population studied (low-risk patients with blunt head trauma, on anticoagulation, greater than 18 years of age), intervention (observation vs repeat imaging), and outcome (delayed ICH).
2. Was the search for relevant studies details and exhaustive?	The search for relevant studies was excellent as they utilized a research librarian, performed a reasonable extensive literature search of MEDLINE, Embase, and Cochrane Library using various search terms. They also had independent assessments for inclusion and quality of studies by three independent reviewers and used a consensus model.
3. Were the primary studies of high methodological quality?	Unfortunately, of the 12 studies used, 10 were qualified as “good” 4 were prospective 2 were of poor quality. No consistent repeat head CT was the cause of these studies being classified as poor quality. Overall probably low to moderate quality.
4. Were the criteria for study inclusion pre-determined and clearly stated?	Yes, the inclusion criteria were: English speaking, 18+ year old, blunt head trauma while on anticoagulation.
5. Did the authors adequately assess the quality of the included studies?	Yes, see table 2 for assessment of the quality of included studies. In this chart, for each article, authors analyze and rate study quality, representativeness, selection of non-exposed cohort, ascertainment of exposure, comparability of cohort, assessment of outcome, if follow-up was long enough and the adequacy of follow-up. Their quality assessments included the use of PRISMA guidelines and the Newcastle-Ottawa Scale
CLINICAL IMPORTANCE	
6. What were the overall results of the review? <i>(Are the results of all included studies clearly displayed? Are the results similar from study to study? Is there a clinical</i>	Overall, of 5,289 patients included, there was delayed ICH in 25 patients on DOACs with a pooled risk of 2.43% (95%CI 1.31-3.88) and 44 patients on warfarin with a pooled risk of 2.31% (95%CI 1.26-3.66). when compared to patients not on anticoagulants 0.4% therefore, The absolute risk reduction (ARR) is 2.43%-0.4 = 2.0% 1/ARR= 1/.02= NNT = 50. Fifty patients would need to

<p><i>bottom line? If the study results combined, was it appropriate to do so?)</i></p>	<p>be observed to identify 1 delayed ICH</p> <p>There was no statistical difference between ICH in DOAC and Warfarin groups. 69 total patients developed delayed ICH. OR 0.89 (95%CI 0.44-1.81).</p> <p>Overall, 4 patients required neurosurgical intervention. 10 patients died from complications related to bleeding. Fifty-nine of sixty-nine patients (86%) who suffered delayed ICH, had no change in their clinical course, while 2 patients on DOAC and 8 patients on warfarin died from complications after delayed ICH.</p> <p>The mortality rate was low, but the overall crude risk of death from delayed ICH among the DOAC and warfarin patients combined was 0.33% (10 of 3,051), and was lower in patients on DOAC (0.16%) than that in patients on warfarin (0.45%).</p>
<p>8. Were the results similar from study to study?</p>	<p>Interestingly, the studies comparing the risk of delayed ICH in patient taking DOAC vs warfarin have been inconsistent. I think it was appropriate to combine study results, because in the end, there was no statistical difference between ICH in DOAC vs warfarin groups. The level of heterogeneity in the studies was considered moderate to substantial The I² for the percentage of delayed ICH for DOACs was 46.4% (95% CI 0.0-72.6%) and the I² for the percentage of delayed ICH for warfarin was 60.4% (95% CI 23.4-79.5%).</p>
<p>APPLICABILITY</p>	
<p>9. How can I best interpret the results to apply them to the care of my patients?</p>	<p>I think this article did a great job in demonstrating and quantifying that the risk of delayed ICH is low. However, at the end of the day, there were some patients that ended up needing neurosurgical intervention and/or dying from delayed ICH. Thus, the risk is not negligible and a patient-centered approach is appropriate since guidelines/risk factors have not been clearly outlined regarding what specific interventions (admission, obs, repeat CT etc.) reduce harms.</p>
<p>10. Were all patient important outcomes considered?</p>	<p>Mostly yes. In this study, primary outcome was development of delayed ICH. Secondary outcomes included neurosurgical bedside procedures to measure intracranial pressure, operative intervention, and mortality.</p> <p>The study did not consider if there any patients with delayed ICH seen on further imaging days to weeks after initial insult.</p>
<p>11. Are the benefits worth the costs and potential risks?</p>	<p>Uncertain. No economic analysis. Are benefits worth the costs of observation in the ED if able to diagnose delayed ICH in this patient population? Furthermore, radiation risk of head CT is negligible considering the demographics of the population studied.</p>

Limitations:

- There were no randomized studies on this topic. The review was limited to retrospective case series and nonrandomized prospective observational studies.
- The risk of reporting and publication bias was inherent in all included studies.
- Some studies did not perform repeat head CTs on all patients.
- The influence of concomitant antiplatelet medications on the risk of delayed ICH is not accurately reflected by our systematic review and the use of reversal agents was rarely reported.
- Compliance with anticoagulation was not reported in any studies.
- INR values were inconsistently recorded.
- The presence of other injuries was not discussed.

Clinical Bottom Line:

More data needs to be collected. This study demonstrates that the risk of delayed ICH is low, and even in those who do have a delayed ICH, it usually does not end up being clinically significant.

Would taking a patient-centered approach that allows discharge of those with excellent home and follow-up care help to reduce admission rates and unnecessary CT's. in patients?