

Critical Review Form Meta-analysis

PGY-2

HYPERLINK "<http://pmid.us/33766725>" **Puzio TJ, Murphy PB, Kregel HR, et al. Delayed Intracranial Hemorrhage after Blunt Head Trauma while on Direct Oral Anticoagulant: Systematic Review and Meta-Analysis. J Am Coll Surg. 2021 Jun;232(6):1007-1016.e5.**

Objectives: "to evaluate the risk of delayed ICH [intracranial hemorrhage] after a normal CT scan in patients on DOACs [direct oral anticoagulants] who suffered blunt head trauma." (p. 1007)

Methods: This systematic review and meta-analysis included studies that enrolled adult patients (≥ 18 years) suffering blunt head trauma who were on anticoagulation and specifically reported outcomes in patients on DOACs. Only English-language studies were included. Case reports and conference abstracts were excluded. A literature search of MEDLINE, Embase, and the Cochrane Library was performed by a medical librarian from inception to June 2020. Titles and abstracts were reviewed by 2 reviewers; articles selected for full review were analyzed by 3 reviewers and the decision to include each article was made by consensus.

The primary outcome was the development of a delayed ICH. Secondary outcomes were neurosurgical procedures to measure intracranial pressure, need for operative intervention, and mortality.

Out of 5719 articles identified by the literature search, 72 underwent full review and 12 were ultimately included. Four of these studies were prospective and 8 were retrospective. They comprised a total of 5289 individual patient encounters; in 1263 encounters (23.9%) the patient was taking a DOAC, while the patient was on warfarin in 1788 (33.8%) cases. Ground level fall was the mechanism of injury in 92% of cases.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Mostly yes. This review seeks to evaluate risk of delayed ICH in patients with minor head injury on anticoagulation, as well as the need for neurosurgical intervention and mortality. While this question is sensible, the review does not address what measures should be taken to mitigate this risk (admission, observation, home observation, routine repeat CT scan).
2.	Was the search for relevant studies detailed and exhaustive?	No. While a medical librarian performed a literature search of MEDLINE, Embase, and the Cochrane Library, there was no search of SCOPUS, Google Scholar, CINAHL, conference proceedings, or the gray literature (publication bias) .

3.	Were the primary studies of high methodological quality?	No. The authors report that 10 studies qualified as having "Good quality" despite only 4 of these being prospective, self-reporting of outcomes in 3 studies (i.e. no routine repeat CT scan), and an inability to report adequate follow-up in 5 of these studies. Overall, while some of these studies are of high quality, many of them are of low to moderate quality.
4.	Were the quality assessments of the included studies reproducible?	Yes. Quality was assessed using the Newcastle-Ottawa Scale for non-randomized trials. "Good quality" studies met 3 or 4 criteria in the selection domain, 1 or 2 criteria in the comparability domain, and 2 or 3 criteria in the outcome/exposure domain. "Fair quality" studies met 2 criteria in the selection domain, or 1 or 2 criteria in the comparability domain, or 2 or 3 criteria in the outcome/exposure domain. "Poor quality" met 0 or 1 criteria in the selection domain or 0 criteria in the comparability domain, or 0 or 1 criteria in the outcome/exposure domain." (pp. 1008-1009)
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> Delayed ICH was observed in 25 patients on a DOAC, for a pooled risk of 2.43% (95% CI 1.31-3.88%). Delayed ICH was observed in 44 patients on warfarin, for a pooled risk of 2.31% (95% CI 1.26-3.66%). Four patients required a neurosurgical intervention, although the authors do not report how many of these were on a DOAC vs. warfarin. The overall crude rate of mortality was 0.16% in the DOAC group and 0.45% in the warfarin group.
2.	How precise are the results?	See above.
3.	Were the results similar from study to study?	The I ² for the percentage of delayed ICH for DOACs was 46.4% (95% CI 0.0-72.6%) and the I ² for the percentage of delayed ICH for warfarin was 60.4% (95% CI 23.4-79.5%). These values suggest a moderate to substantial degree of statistical heterogeneity .
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	While the risk of delayed intracranial hemorrhage among patients taking a DOAC or warfarin is not negligible (2.43% vs. 2.31%), very few of these patients died or required any neurosurgical intervention. Further, there is no evidence that observation in the ED or hospital, or routine repeat CT scanning, would reduce the number of patients with a patient-centered, outcome .

2.	Were all patient important outcomes considered?	Mostly yes. The patients considered the risk of delayed ICH, need for neurosurgical intervention, and mortality. They did not assess other changes in management, such as holding or reversing anticoagulation, and were not able to assess cost in this systematic review.
3.	Are the benefits worth the costs and potential risks?	Uncertain. As noted above, the risk of death or need for neurosurgical intervention was low and this study was not able to assess whether routine observation or repeat CT scanning would have any impact on these outcomes.

Limitations:

- 1. Only English-language studies were included. It is unclear how many studies were excluded on this basis.**
- 2. Conference abstracts were excluded, raising the risk of [publication bias](#).**
- 3. Despite reporting "Good quality" for 10 of the included studies based on their criteria, the studies were largely of moderate to poor quality.**
- 4. The authors report that 4 patients required a neurosurgical intervention, but do not specify how many of these were taking a DOAC vs. warfarin.**

Bottom Line:

This systematic review and meta-analysis found that the risk of delayed intracranial hemorrhage among patients taking a DOAC or warfarin was 2.43% and 2.31%, respectively. Neurosurgical intervention was only required in 4 patients, but the authors fail to report which group these patients belonged to. The overall crude rate of mortality was 0.16% in the DOAC group and 0.45% in the warfarin group.