

## Clinical Practice Statement

### ***Do patients on Direct Oral Anticoagulants (DOACs) require repeat imaging and a period of observation after a head injury with an initial negative CT?***

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#### **Summary Recommendation:**

There is substantial clinical uncertainty regarding the management of head injured patients taking DOACs for delayed intracranial hemorrhage (ICH) as there are no high-quality studies evaluating this question. DOACs have been generally shown to have a reduced rate of mortality, hemorrhagic stroke, and intracranial hemorrhage compared with vitamin K antagonists (VKAs). While there is substantial evidence showing that delayed ICH after head injury is very rare with VKAs this cannot be directly extrapolated to patients on DOACs.(1) Thus, in the absence of high-quality studies evaluating delayed ICH with DOACs after head injury, the clinician should carefully evaluate the risks and benefits of immediate discharge or a period of observation and repeat CT.

#### **Introduction:**

Anticoagulants (ACs) are used for a wide variety of medical purposes such as atrial fibrillation and the treatment (and prevention) of veno-thromboembolic (VTE) disease. While previously the most common oral anticoagulation medicines were VKAs, there is now a burgeoning new field of anticoagulants. These are collectively referred to as DOACs. Patients who take anticoagulants have a higher risk of ICH, an increased severity of ICH, and increased likelihood of death from ICH. (2) This is compounded by the fact that most patients on ACs tend to be elderly and thus have a more fragile vasculature compared to a younger population.(3,4) To date, there have been no high-quality studies that have examined the rate of delayed spontaneous intracranial hemorrhage in patients on DOACs after a traumatic head injury.

#### **Methods:**

We performed a PubMed search utilizing the search terms “DOAC, NOAC, Direct Oral Anticoagulant, Novel Oral Anticoagulant, traumatic brain injury, and delayed intracranial hemorrhage”. We then used the AAEM methodology literature review criteria to assess each paper. The highest quality data available was synthesized to examine this question.

#### **Executive Summary:**

The use of DOACs has increased over the last several years due to its improved safety profile and lack of the need for monitoring. A large meta-analysis performed by Ruff et al showed that DOACs had a reduced rate of mortality,

hemorrhagic stroke, and intracranial hemorrhage. (5) While this shows that DOACs are generally safer compared to VKAs, the safety profile cannot be extrapolated to traumatic injuries. However, DOACs have been shown to have a lower rate of immediate traumatic ICH compared to VKAs. (6) Additionally, the rate of immediate traumatic ICH for patients on DOACs is similar to elderly patients not on AC who had a mild head injury. (7)

We performed a systematic review that examined seven studies evaluating DOAC use and delayed ICH after TBI. All the studies found were from 2017 to the present highlighting the new interest in this question. The results are listed in Table 1.

**Table 1. Summary of Results**

Authors	Design	Number of patients on DOACs	Delayed ICH	Clinically relevant ICH (Intervention/death)
Barmparas et al (8)	Multi-centered Retrospective	249	2	0
Cipriano et al (9)	Single centered prospective	85	2	1*
Chenoweth et al (10)	Multi-centered prospective	37	0	0
Bauman et al (11)	Single centered retrospective	35	1**	0
Mann et al (12)	Single centered retrospective	30	1	0
Marcia et al (13)	Single centered retrospective	19	2	Unclear***
Verschoof et al (14)	Multi-centered retrospective study	17	0	0

\*The single mortality in the Cipriano study was due to a delayed ICH which developed eight days after a mild TBI.

\*\*The one delayed ICH was questionably an artifact as a subsequent MRI showed no ICH and the patient was discharged without any negative consequences.

\*\*\*Unable to distinguish if the two patients were a progression of an immediate ICH or a delayed ICH as the study aggregated progression of ICH and delayed ICH cases in the same result summary.

### **Conclusion:**

Delayed ICH for patients taking DOACs is a rare event. In our review, we found only eight patients with delayed ICH out of a total of 472. Further, only one patient had a clinically important outcome (death). This was complicated by the fact that the delayed ICH occurred eight days after the initial mild TBI. Limitations to the data included: small sample sizes, case series study design, and retrospective studies accounting for the majority of enrolled patients. While delayed ICH has been shown to be rare overall for patients on VKAs, the data is currently not strong enough to state conclusively that delayed ICH for patients on DOACs is rare enough to preclude repeat imaging and observation.