Critical Review Form
Prognosis

Delayed intracranial hemorrhage after blunt trauma: are patients on preinjury anticoagulants and prescription antiplatelet agents at risk? *J Trauma* 2011; 71: 1600-4

Objectives: **To assess incidence of delayed intracranial hemorrhage (ICH) seen on repeat 6-hour CT scan in patients with no traumatic findings on CT1 and a normal or unchanged interval neurologic examination.**

Methods: **Retrospective chart review of patients presenting to a Level I trauma center between January 1, 2006 and August 31, 2009 with head injury taking anticoagulants or antiplatelet agents. Inclusion criteria were:**

1) **Age ≥ 15 years.**
2) **Blunt mechanism of injury**
3) **Preinjury use of an anticoagulant or antiplatelet agent (warfarin, clopidogrel, heparin, enoxaparin, or dipyridamole and aspirin in combination).**

Patients taking aspirin alone were excluded, as were those taking warfarin with an INR < 1.3. Patients underwent routine initial head CT, and those with negative results were admitted for 6 hours of observation followed by repeat head CT.

Head CT results were obtained from the medical record and were classified as positive, negative, or equivocal. Positive scans were those demonstrating acute ICH, including subarachnoid or intraparenchymal hemorrhage, subdural or epidural hematoma, or parenchymal contusion. Equivocal scans were considered positive. To assess for reliability, all positive repeat CT scans (following negative initial CT) were then reviewed by a second, board-certified radiologist experienced in trauma radiology, who was blinded to the initial interpretation and to all clinical details.

An inquiry was made to the San Diego County Medical Audit Committee, which reviews all deaths and readmissions in the area, to determine if any patients suffered readmission of death related to head injury. The study institution's Trauma Registry was also reviewed to identify patients with progression of neurologic insult or unexpected readmission.

Guide		Comments
I.	**Are the results valid?**	
A.	**Was the sample of patients representative?** *In other words, how were subjects selected and did they pass through some sort of "filtering" system which could bias your results based on a non-representative sample. Also, were objective criteria used to diagnose the patients with the disorder?*	Yes, the patients were representative, as they included patients on anticoagulant therapy with minor head injury. The patients represented all patients with traumatic blunt head trauma, on anticoagulant or antiplatelet therapy, presenting to a level I trauma center. There were no true objective criteria to determine the presence of trauma to the head. Filter #1: This study included patients presenting to a level I trauma center. This would likely include more severely injured patients than would be seen in a community hospital, increasing the incidence of immediate and delayed ICH.
B.	**Were the patients sufficiently homogeneous with respect to prognostic risk?** *In other words, did all patients share a similar risk during the study period or was one group expected to begin with a higher morbidity or mortality risk?*	Yes, as these patients all had relatively minor head injury with a normal initial CT scan. Certain risk factors would put some patients at higher risk of adverse outcome, including advanced age, more elevated INR, mechanism on injury, loss of consciousness associated with the traumatic event, and more severe symptoms. Table 1 lists many of these risk factors, including: Mean age 75 years Loss of consciousness in 131 (35.7%) Mean Injury Severity Score 4.9 Focal deficit at admission in 17 (4.0%) Concomitant ASA use in 119 (28.1%)
C.	**Was follow-up sufficiently complete?** *In other words, were the investigators able to follow-up on subjects as planned or were a significant number lost to follow-up?*	No. While all 424 patients were observed for at least 6 hours, 62 (15%) did not receive a second CT. These would likely comprise low-risk patients with no change in neurologic status and no concerning symptoms who would be unlikely to develop delayed ICH. However, there is the risk that delayed ICH was missed in some of these patients (though these would likely be clinically insignificant).
D.	**Were objective and unbiased outcome criteria used?** Investigators should clearly specify and define their target outcomes before the study and whenever possible they should base their criteria on objective measures.	Yes. Outcome criteria included the development of ICH on repeat CT scan, defined as the presence of "subarachnoid hemorrhage, intraparenchymal hemorrhage, parenchymal contusions, subdural hematoma, and epidural hematoma." (p.1601).

II.	What are the results?	
A.	**How likely are the outcomes over time?**	• Between Jan 2006 & Aug 2009 there were 564 head injury patients, but 64 had INR < 1.3 and 64 (15%) had ICH on the first CT leaving 424 for this analysis. • 62/424 (14.6%) refused the second CT. • Standing level falls represented 84% of the head injury mechanisms and the mean age was 75 years. • 0/15 with mental status changes after the first CT had an ICH on the second CT. • There were four (1%; 95% CI 0.4%-2.4%) positive repeat CT scans in patients with normal initial CT scan. • Of a total of 289 patients on warfarin included in the study, there were four (1.4%; 95% CI 0.5%-3.5%) positive repeat CT scans (representing all positive cases). • All four positive CT2 cases were > 80 years old • None of these patients (0%; 95% CI 0%-1%) required neurosurgical intervention. One patient was initially given FFP, however his INR changed from 3.9-3.3, and it was determined by neurosurgical consultation that correction of the INR was unnecessary.
B.	**How precise are the estimates of likelihood?** *In other words, what are the confidence intervals for the given outcome likelihoods?*	See above.
III.	**How can I apply the results to patient care?**	
A.	**Were the study patients and their management similar to those in my practice?**	No. While the study institution (Scripps Mercy Hospital, San Diego, CA) is a US level I trauma center and should see a similar level of acuity in trauma patients to our institution, at our institution we do not routinely admit patients with head injury and anticoagulant/antiplatelet therapy, nor do we routinely obtain repeat CT scans on these patients. There is no protocol requiring all of these patients to undergo an initial head CT, although I suspect the majority do. All other management strategies would be expected to be similar.

B.	**Was the follow-up sufficiently long?**	No. The study sought to assess the incidence of delayed ICH in patients 6 hours after initial negative CT scan. The mean time to repeat CT was 8.8 hours (SD 10.2 hours). The optimal time for observation and repeat CT scan has not yet been determined, and a short protocol such as this does run the risk of missing delayed ICH beyond this window. The review of the San Diego Medical Audit Committee and Trauma Registry may help prevent missing these delayed injuries.
C.	**Can I use the results in the management of patients in my practice?**	Yes. The current study does not support the practice of routine 6-hour observation and repeat CT scanning in these patients, given the low incidence of delayed ICH (1%), and the lower incidence (0%) of patients requiring neurosurgical intervention.

Limitations

1) **This was a retrospective chart review without methods (Gilbert 1996, Worster 2004) and with the inherent risks of selection bias and reviewer bias, and loss to follow-up.**

2) **62 of 424 patients observed (15%) did not undergo repeat CT scanning as described in the protocol. While these patients were likely at low risk, this large loss to follow-up could potentially bias the results and underestimate the rate of delayed ICH. The outcome of these 62 patients is not described. There is no sensitivity analysis performed to determine the potential significance of this.**

3) **Failure to follow STROBE guidelines for reporting in observational trials by not reporting 95% CIs.**

4) **A blinded outcome assessor was used, but only those CT scans interpreted as positive were reviewed. This could underestimate the incidence of delayed ICH, though likely did not affect the incidence of neurosurgical intervention.**

5) **Repeat head CT was performed after 6 hours of observation. While the appropriate duration of follow-up has yet to be determined, many physicians may feel a 6-hour protocol is too brief to detect most clinically significant delayed ICHs.**

6) **No details about unmeasured confounding predictor variables such as the fall mechanism, injury or illness severity, or geriatric syndromes such as frailty or**

functional decline that could affect initial CT ordering and ED length-of-stay decisions.

7) **No assessment of CT-head injury rules (New Orleans, CHIP, NEXUS-II, and Canadian) which might have been helpful to predict delayed CNS bleeding risk.**

Bottom Line

This retrospective chart review identified 424 patients on anticoagulant or antiplatelet therapy who were observed following a negative CT scan, of whom 362 had repeat cranial CT scans performed approximately 6 hours after admission. Of these, 4 (1%; 95% CI 0.4%-2.4%) were found to have delayed ICH; all 4 of these cases occurred in the 294 patients on warfarin (1.4%; 95% CI 0.5%-3.5%). None of these patients required neurosurgical intervention. Unfortunately, there was a large loss to follow-up rate in this study (15%), and the fate of these patients is mentioned nowhere in the study. The results suggest a low rate of delayed ICH at 6 hours and even lower rate of ICH requiring neurosurgical intervention, suggesting a protocol of observation with routine CT scan at 6 hours is unnecessary. This study does not address issues of more prolonged follow-up and the risk of delayed ICH beyond 6 hours.