Critical Review Form
Prognosis

Management of minor head injury in patients receiving oral anticoagulant therapy: a prospective study of a 24-hour observation protocol, *Ann Emerg Med* 2012; 59: 451-455.

Objectives: "Patients receiving warfarin who experience minor head injury are at risk of intracranial hemorrhage, and optimal management after a single head computed tomography (CT) scan is unclear. We evaluate a protocol of 24-hour observation followed by a second head CT scan." (p. 451)

Methods: Prospective, observational, consecutive patient study from single level II trauma center in Ancona, Italy from January 2007 to March 2010. Included patients were aged 14 years or older with minor head injury, defined as a head injury and a presenting Glasgow Coma Scale (GCS) score of 14 to 15, on oral anticoagulation therapy for at least one week. Patients were included regardless of the presence or absence of loss of consciousness. Additionally, to be included patients had to present within 48 hours of trauma and have an Injury Severity Score less than 15. Patients were excluded if the initial CT scan revealed an acute traumatic intracranial injury ("subdural, epidural, or parenchymal hematoma; subarachnoid hemorrhage; cerebral contusion; or depressed skull fracture") (p. 452). All eligible patients were admitted to the ED Observation Unit for 24 hours, at which time a 2nd CT scan was performed. All CT scans were read by staff neuroradiologists. All patient information was collected prospectively by the ED physician caring for the patient.

Outcome measures were assessed by review of the electronic medical records by the two investigators (V.G.M. and M.L.) and included:

1) **Presence of acute traumatic intracranial injury on the 2nd CYT scan, as previously defined**
2) **Death**
3) **Admission for CT abnormality**
4) **Neurosurgical intervention**
5) **Readmission within 30 days for chief complaint related to the initial head injury.**

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. This was an observational study performed at a level II trauma center. These were patients with minor head injury, GCS 14-15 (all included patients had a GCS of 15), presenting within 48 hours of trauma, on oral anticoagulant therapy, with an initial normal CT scan. Patients with a high injury severity score (ISS) $\geq$ 15 were excluded. There were no true objective criteria used to determine the presence of trauma to the head. Filter #1: this was a **level II trauma center with a lower acuity of trauma patients** than our institution (possible *spectrum bias*). Filter #2: patients with a high ISS were excluded, again **selecting for lower acuity patients**. While this is likely the subset of patients with whom we are concerned, as higher acuity patients would likely have injuries requiring admission and observation, it would be difficulty to apply the results to higher acuity patients in determining the need for serial CT scan after admission.
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. However, certain risk factors would put some patients at higher risk of adverse outcome, including advanced age, more elevated INR, mechanism of injury, loss of consciousness associated with the traumatic event, and more severe symptoms. Median age 82, range 60-93 GCS of 15 in 87 (100%) Loss of consciousness in 16 (18%) Posttraumatic amnesia in 4 (5%) Vomiting in 3 (3%) Severe headache in 3 (3%) INR > 3 in 8 (9%) INR $\leq$ in 79 (91%) INR 2.5-3 in 53 (61) INR < 2.5 in 19 (22%) INR < 1.5 in 7 (8%) No patients were on concomitant antiplatelet therapy.

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. Of the 97 patients included, 10 declined the 2nd CT scan, leaving only 87 patients with the intended follow-up. While none of these 10 developed a clinically significant bleed, the method of follow-up used to determine this is not noted in the article; the manuscript states, "none were readmitted within 30 days." It is unclear if this was determined by medical records review (with the limitation that patients may present to outside hospitals or may die and not be seen in any hospital), or if telephone follow-up was employed. These 10 patients were not included in the statistical analysis. The same limitation applies to patients discharge after a 2nd normal CT scan; two patients are identified as having delayed SDH following discharge, and it is unclear if these were identified by review of the records, or if any of these patients were contacted for follow-up.
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. The outcome was any ICH noted on the repeat (24 hour) CT scan, as read by a staff neuroradiologist. At many institutions, head CT scans are interpreted by non-neuroradiology trained physicians or by residents or fellows. Other outcomes included death, 30-day readmission related to the initial head trauma, or neurosurgery for an abnormal CT. Additionally a more patient-oriented outcome could be used, such as the need for neurosurgical intervention or other significant change in management (discontinuation of anticoagulation, administration of vitamin K or FFP). Only one (1.1%) of the 5 patients identified required neurosurgical intervention, though "neurosurgical intervention" is not well-defined (craniotomy, craniectomy, burr hole placement, ICP monitoring, mannitol/hypersaline administration). It is unclear if the remaining patients required any change in therapy based on the findings.
II.	**What are the results?**	

A.	**How likely are the outcomes over time?**	• Over 3 years 4992 head injury patients, but 390 were moderate or severe (severe being undefined) leaving 4602 mild head injury patients of whom 2.5% were on anticoagulation. • Mechanism of head injury was accidental trauma in 79% and syncope in 21%. • 5 (6%; 95% CI 1%-11%) of the 87 patients receiving the 24-hour head CT had ICH noted. Including the 10 that refused the 2nd CT as "no ICH at 24 hours", this would be 5 (5%; 95% CI 2%-12%) of 97. • Only 1 (1%; 95% CI 0.2%-6.2%) of 87 patients required neurosurgical intervention. Alternately, this represents 1 (1%; 95% CI 0.2%-5.6%) of 97 total observed patients. • Two (2%; 95% CI 0.5%-5%) additional SDHs were identified in follow-up • The greatest predictor of delayed ICH was an INR greater than or equal to 3 (relative risk=14; 95% CI 4 to 49). • Most common risk factors for ICH included evidence of trauma above the clavicles (85%) and LOC (18%).
B.	**How precise are the estimates of likelihood?** *In other words, what are the confidence intervals for the given outcome likelihoods?*	See the 95% CI's 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, management in the study was very dissimilar. Currently at our institution standard management includes discharge home after a normal initial CT scan. Patients in the study were admitted for standard 24-hour observation and routine 24-hour CT scan. This raises the possibility of detecting clinically insignificant injuries that would not be detected in our environment. This study was performed at a level II trauma center where one would expect lower acuity patients. In addition, patients were excluded for ISS greater than or equal to 15. One could consider including only low-risk trauma patients in this protocol (as is suggested) and expect patients to be similar.

		Patient age, likely a prognostic factor, is likely similar (median age 82). However, none were on concomitant antiplatelet therapy (unsure what percentage of my patients are on AP agents) and there is little information on other comorbidities (which may or may not influence the risk of outcome).
B.	**Was the follow-up sufficiently long?**	Uncertain. Given that the study sought to address the sensibility of current European guidelines (24 hours of observation followed by repeat CT scan), the duration of follow-up was adequate. An additional two patients were identified with delayed SDH beyond 24 hours (readmitted 2 and 8 days later). These patients would be missed by the current guidelines.
C.	**Can I use the results in the management of patients in my practice?**	Yes. This study looked at a surrogate outcome (ICH noted on repeat CT scan), rather than patient-oriented outcomes (death, neurologic disability). Only one patient out of 87 required neurosurgical intervention (1.1%), which is rather low; it is also possible that this patient suffered neurologic deterioration prior to repeat CT and would have been detected without the protocol in place. It is also unclear if the other four patients required any important changes in management, since two were discharged without any further therapy. The 95% CI for the 1.1% value extends to 6.2%; a larger study with more narrow CI's would be beneficial to further define the actual risk. A randomized controlled trial using observation and 24 CT scan as a treatment (compared to standard therapy of discharge for home observation), would be useful in determining if any change in patient-important outcomes (death, neurologic disability) would result from serial CT scanning. In addition, an evaluation of the cost associated with this protocol would help determine its feasibility.

Limitations

1) **The primary limitation includes the use of a surrogate outcome (any traumatic intracranial lesion) as opposed to a patient-important outcome (i.e. death or neurologic disability). Only patient out of 87 required a neurosurgical intervention; it is noted that one of the five patients with a positive repeat CT scan had a deterioration in neurologic status, but it is not noted whether this was the patient who required neurosurgical intervention.**

2) **Neither the clinicians recording data prospectively, nor the investigators reviewing charts for outcome measures was blinded to the study objectives. There is no analysis of inter-observer agreement between the investigators for the outcomes of interest. (Gilbert 1996, Worster 2004)**

3) **None of the patients included were taking concomitant antiplatelet agents, which could underestimate the risk of delayed intracranial hemorrhage. Concomitant antiplatelet therapy in patients taking oral anticoagulants in the US ranges from 19.4-38.5%. (Shireman 2004) (Johnson 2007)**

4) **There is no cost-analysis performed to justify the observation protocol. A subsequent editorial (Li 2012) calculated the average cost using data from this article and the article by Kaen et al (Kaen 2010). Utilizing the European protocol (2 CT scans and 24 hours of observation), the cost needed to save one patient would be $1,016,960 in the US and $105,280 in Canada (adjusted 2011 dollars).**

5) **No assessment of test-treatment threshold to identify an appropriate level below which continued imaging would cause more harm than good. (Pauker 1980)**

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

The overall risk of developing a delayed intracranial hemorrhage was found to be 6%, with a fairly wide 95% CI (1%-11%). Based on this risk, the authors conclude that the data support the recommendation for routine observation and repeat CT scan at 24 hours. However, only one of the five patients with delayed ICH required any neurosurgical intervention (1%, 95% CI 0.2%-6.2%), and this patient was noted to have a declining neurologic status during the period of observation. Other less expensive strategies, including inpatient or home observation monitoring any changes in neurologic status (without routine repeat head CT) or telephone follow-up could potentially lead to similar outcomes without the associated cost.