Critical Review Form
Prognosis

The value of sequential computed tomography scanning in anticoagulated patients suffering from minor head injury, *J Trauma.* 2010; 68: 895-898.

Objectives: **"To evaluate the need of performing a control CT scan in patients on anticoagulation treatment who showed neither intracranial pathology on the first CT scan nor neurologic worsening during the observation period." (p. 895)**

Methods: Prospective, consecutive patient study from October 2005 to December 2006 at Hospital 12 de Octubre in Madrid, Spain. Included patients were older than 16 years, suffering minor head injury within 48 hours of presentation with GCS 14-15, on anticoagulant therapy (defined as current treatment with heparin or warfarin), with a normal initial head CT. Loss of consciousness and posttraumatic amnesia were NOT used as exclusion criteria. All eligible patients were admitted for 24 hours of observation, with serial neurologic examinations performed every 4-6 hours. A control CT scan was performed on all patients 20-24 hours after the initial CT scan. Demographic data and subsequent examination data were obtained by neurosurgical residents. CT scans were interpreted by radiology or neurosurgery staff. Findings on control CT scans were compared to the initial CT and classified as unchanged or worsened (defined as the presence of any sign of intracranial bleeding).

	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 the equivalent of a level I trauma center in Spain. Patients included had had a minor head injury with GCS 14-15, on anticoagulant therapy, with initial normal CT scan. No true objective criteria were used to determine the presence of head trauma. Filter #1: this was a level I-equivalent trauma center, similar to our practice environment. While this could lead to the inclusion of higher acuity patients than many institutions see, the limitations on GCS and initial CT scan findings should ensure a lower level of acuity among included patients. Filter #2: the study included patients admitted to the neurosurgical unit, rather than all ED patients. However, the authors state that at their institution, "a CT scan is obtained in all patients with coagulopathy, who after being placed under close observation during the first 24 hours after head injury, should also have a control CT scan before discharge." They infer that it is routine practice for these patients to be admitted to their unit.

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, loss of consciousness associated with the traumatic event, and more severe symptoms. INR levels were not included for all patients. This would have been an important prognostic factor to consider. Median age 76 GCS of 15 in 122 (89%) GCS of 14 in 15 (11%) Severe headache in 34 (25%) Vomiting in 27 (20%) Loss of consciousness in 14 (10%) Posttraumatic amnesia in 6 (4%) Seizure in 2 (1.7%) Concomitant anticoagulation in 3 (2%)
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?*	Yes. All patients were followed for ~24 hours with repeat CT scan prior to discharge, as per protocol. There is no mention of any patients being lost to 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. Delayed intracranial bleeding after normal initial CT scan was the primary outcome. There is no specific mention of the need for neurosurgical intervention or other change in management (reversal of anticoagulation, vitamin K or FFP administration) being measured as outcomes, though these data are included. In addition, death and neurologic disability were not measured. Head CT scans were read by "the radiology or neurosurgery staff" (p. 896). It is not clear if formal reads were used, or if neuroradiology trained radiologists were involved in interpretation. No measurement of inter-rater agreement was examined.
II.	**What are the results?**	

A.	**How likely are the outcomes over time?**	• 137 patients analyzed with fall (89%) the predominant mechanism of injury followed by MVA (5%) or assault (3%). • Mean INR 3.8. • Median time to CT#2 was 20 hours. • 2/137 (**1.5%;** 95% CI 0.4%-5%) **found to have hemorrhagic lesions on control CT scan – both were among the 3 patients who were also on an antiplatelet agent and among the 10% with loss of consciousness**. • **0** (0%; 95% CI 0%-3%) **required change in management based on control CT scan findings.** • One of the two ICH patients was a 67 year old man on warfarin and aspirin with an INR of 3.1; control CT showed minimal intraventricular hemorrhage. He showed no neurologic deterioration and anticoagulant therapy was not withheld. Repeat CT 24 hours later showed no change, and he was discharged 48 hours after admission. • The other patient was a 74 year old man on warfarin and aspirin with an INR of 2.88; control CT showed a discrete subarachnoid hemorrhage over the convexity of the right cerebral hemisphere. His anticoagulation was not withheld and a repeat CT scan prior to discharge showed no changes. • The difference in incidence of bleeding between patients with and without concomitant antiplatelet use was statistically significant (ARR -67%; p=0.01) as was the difference between patients with and without loss of consciousness (ARR -14%; p=0.004).
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 is dissimilar. At our institution, anti-coagulated patients with a normal initial head CT are discharged home, while the study involved 24-hour admission for these patients with routine repeat head CT at 24 hours. Given that only 2 clinically insignificant injuries were found using this protocol, this difference in management would likely not result in different outcomes based on this study. The study was conducted at level I-equivalent trauma center in Madrid, Spain. One would expect similar trauma acuity to our institution. The inclusion of only low acuity head injury patients is sensible (GCS 14-15) and would have to be considered when applying the study results. Patient age, a significant prognostic factor, is likely similar (median 76 years). The low rate of concomitant antiplatelet agent therapy in the population is dissimilar to rates seen in the US (see below), which would underestimate the incidence of delayed intracranial hemorrhage.
B.	**Was the follow-up sufficiently long?**	Uncertain. Given that the purpose of the study was to evaluate the current European guideline recommendation (24 hours of observation followed by repeat head CT), the 24-hour follow-up used in the study is sensible. Longer follow-up would help to determine the incidence of delayed injuries beyond 24 hours, but such injuries would still be missed using the current guidelines.
C.	**Can I use the results in the management of patients in my practice?**	Yes. The results of study are promising; no patients in the study suffered clinically significant ICH after 24 hours of observation. This supports current practice of routine discharge in low-risk anti-coagulated patients with a normal initial head CT. The size of the study limits easy applicability, given that the 95% CI for clinically significant ICH ranged from 0%-3%. Were the rate truly 3%, a cost-benefit analysis would be needed to help further guide widespread application.

Limitations

1) The outcome assessors were not blinded to study objectives (detection bias), and likely included the study investigators. Initial CT scans were interpreted by neurosurgical residents, and all of the control CT scans were interpreted by "the neurosurgical team."

2) Failure to follow **STROBE guidelines** for reporting of observational studies:
   a. Setting and location not described.
   b. Missing important demographic data (INR levels).
   c. Primary outcomes poorly defined.
   d. No attempts made to address potential sources of bias.
   e. Measures of precision not included (failure to include 95% confidence intervals).

3) Low rate of concomitant antiplatelet agent use (2.2%), 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) **Underpowered study** with no **modeling**.

5) Uncertain **external validity** (Spanish "unit").

6) No assessment of cost-benefit or **test-treatment thresholds**.

7) Unmeasured confounding variables that could be independently associated with either the risk of ICH or the likelihood of diagnostic testing, including: injury severity, comorbid illness burden, frailty, social support, or physician gestalt.

8) 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

There were only two (1.5%; 95% CI 0.4%-5%) patients with an ICH found on the repeat CT scan, however neither of these patients required any neurosurgical intervention. The authors conclude based on their results that they do not recommend routinely repeating CT scans on anticoagulated patients suffering minor head injury. Interestingly, they note that both of the patients found to have delayed ICH were concomitantly taking aspirin, and felt that a repeat CT should routinely be

performed on such patients. The rate of concomitant antiplatelet therapy in studies in the US has ranged from 19.4-38.5% (**Shireman 2004**) (**Johnson 2007**), suggesting a potentially large number of patients to whom this would apply, and given that neither of these patients required neurosurgical intervention, this recommendation may be premature. The authors do note that larger studies would need to be performed (particularly in this subset) to establish more definitive conclusions.