Critical Review Form

Diagnostic Test

Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of SAH prospective cohort study;
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Objectives: To determine "the sensitivity of modern computed tomography for identifying subarachnoid hemorrhage in neurologically intact patients who present to the emergency department with acute headache, especially when scans are performed within six hours of headache onset". (p. 2)

Methods: Prospective study from November 2000 to December 2009 across 11 Canadian university affiliated tertiary care teaching hospitals which was part of a larger project to develop clinical decision rules for acute non-traumatic headache patients. (Perry 2010) Eligibility criteria included age >15, GCS 15, absence of falls or head trauma in the preceding 7-days, and maximum headache intensity within one-hour after onset. CT's and LP's were obtained at the discretion of the treating clinicians. All patients were assessed by EM attending physicians or residents, who also completed the data forms.

SAH was present if CT demonstrated any subarachnoid blood, if CSF xanthochromia was noted (not using spectrophotometry which 97% of hospitals lack as noted by Edlow 2002), or if > 5 rbc were noted in the final CSF tube with cerebral angiography confirmation of an aneurysm. CT's were interpreted by "qualified local radiologists (a neuro-radiologist or general radiologist)" from third generation multi-slice scanners (from 4 to 320 slices/rotation). For patients with a negative CT who did not have an LP, telephone follow-up at 6-months was planned. If unable to reach by telephone, records from the local neurosurgical center and provincial coroner were reviewed.

Sensitivity, specificity, negative LR and NPV are reported. *A priori* a sensitivity analysis to assess differences between those with and without LP was planned. Based upon assumption of sensitivity 100%, SAH prevalence 7%, and 3% confidence intervals, the investigators planned a total sample size of 2860 patients.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Yes. "The treating physician completed the clinical decision rule study data forms" (p. 2) presumably before the CT and LP results were available.

B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?**	No. The study was limited "by the absence of a single widely accepted standard criterion for subarachnoid hemorrhage." In addition, the authors "excluded many patients in whom no computed tomography was performed. Forcing physicians to order a test would have exposed patients to ionizing radiation and increased healthcare costs. Similarly, not all patients with normal results on computed tomography underwent lumbar puncture." (p. 5) This is the balance between research purity and pragmatic risk aversion.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?**	Undoubtedly, the results of CT and LP influenced decisions about angiography. This bias will falsely increase estimates of sensitivity.
II.	**What are the results?**	
A.	**What likelihood ratios were associated with the range of possible test results?** Population / Sen (95% CI) / Spec (95% CI) / LR^+ / LR^- All Pts. / 93 (89-95.5) / 100 (99.9-100) / ∞ / 0.07 (0.05-0.11) ≤ 6 hours / 100 (97-100) / 100 (99.5-100) / ∞ / 0 (0.00-0.02) > 6 hours / 86 (78-91) / 100 (99.8-100) / ∞ / 0.14 (0.14-0.17)	• 3132 patients were enrolled with mean age 45, 60% female, 8.7/10 headache severity at peak, and 82.1% describing worst headache of life. • SAH was the discharge diagnosis in 7.7%, while benign headache (55.9%) and migraine (20.1%) were more common. • Only 30.4% had CT ≤ 6 hours post-headache onset and only 49.4% had an LP. • CT demonstrated the diagnostic accuracy noted to the left. • In those with CT delayed > 6 hour, delays ranged from 8 hours to 8 days. • 1931 patients required follow up and 1506 were contacted by phone, representing a substantial lost to follow-up. However, "even if we adopt a highly conservative view that a quarter of our patients lost to all follow-up could have experienced a SAH, diagnosed and treated in a different region, or a sudden out of hospital death that was not reported to the coroner. The corresponding negative likelihood ratio for a computed tomography performed within 6 hour rises to only 0.024 (95% CI 0.007 to 0.07)." (p. 5)

		• There were differences between those with and without post-CT LP. Those who had an LP were younger (43 vs. 47), had faster peak of their HA (5.7 vs. 9.4 minutes), more frequent neck pain (39% vs. 35%), and described the "worst headache ever" (92% vs. 76%).
III.	**How can I apply the results to patient care?**	
A.	**Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?**	Probably, ED patients with acute onset HA and newer generation CT scanners.
B.	**Are the results applicable to the patients in my practice?**	Yes, all acute headache patients with clinical concern for SAH.
C.	**Will the results change my management strategy?**	Yes. Although I will still provide patients who have a CT performed less than six hours after the onset of their HA with an for LP to definitively exclude SAH (within the context of existing evidence that suggests CT sensitivity is 90-100% sensitive), I will be more confident that SAH has not been missed when CT is negative in this subset of patients. Those with HA onset > 6 hours before CT still need LP to definitively exclude SAH.
D.	**Will patients be better off as a result of the test?**	Yes, if some acute onset HA patients with concern for SAH (i.e., those with CT <6 hours after HA onset) can avoid the pain, delay and long-term complications of LP without missing SAH.

Limitations

1) **Lack of uniform gold standard for SAH.**

2) **Lack of uniform testing (CT, LP) for all acute onset HA patients, although this pragmatic approach reflects clinical reality. The investigators note that "After enrolling patients at multiple large hospitals across Canada for nearly a decade, and having failed to identify a single false negative, we are confident that such an event is indeed rare." (p. 5)**

3) **Failure to incorporate and reference STARD criteria.**

Bottom Line

CT is highly sensitive for SAH if performed with multi-row third generation scanner with thin slices within 6 hours of headache onset when the scans are interpreted by a qualified radiologist. Beyond 6 hours after headache onset, LP is still required to definitively exclude SAH.