

Critical Review Form

Diagnostic Test

Is the Combination of Negative Computed Tomography Result and Negative Lumbar Puncture Result Sufficient to Rule Out Subarachnoid Hemorrhage?

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Objectives: “To determine the sensitivity and specificity of the strategy of a negative CT scan result of the head and negative result in the final tube of cerebrospinal fluid and the resulting likelihood ratios for ruling out the presence of a subarachnoid hemorrhage in ED headache patients suspected of having a subarachnoid hemorrhage”. (p. 708)

Methods: Prospective consecutive patient study from two academic Canadian ED’s (both probably in Ottawa but not clearly named in the manuscript) from November 2000 to November 2003. Inclusion criteria included age > 15 years, GCS 15, maximal headache intensity within 1 hour of onset and < 14 days before ED presentation, and no head trauma within 7-days. Exclusion criteria included 3 or more similar headaches in preceding 6 months, acute SAH confirmed prior to ED arrival, reassessment of the same headache (previously evaluated with CT and LP), papilledema, previous SAH or brain cancer, new focal neuro deficit, neurologic shunt, or post-LP headache (within 72 hours of LP). All eligible subjects had a telephone follow-up with structured questions (Fig 1, page 709) at least 6 months after their ED visit.

The primary outcome was SAH which was labeled present if any of the following scenarios occurred:

- 1) Subarachnoid blood on CT per final neuroradiology report.
- 2) Xanthochromia in CSF by visual inspection of centrifuged supernatant.
- 3) > 5 rbc/hpf with aneurysm noted on cerebral angiography.
- 4) Autopsy confirming SAH.

If none of these conditions occurred and if a patient did not have a subsequent diagnosis of SAH on follow-up, then they were classified as not having SAH.

Guide		Comments
I.	Are the results valid?	
A.	Did clinicians face diagnostic uncertainty?	Yes, clinicians did not know whether or not the acute headache represented SAH at the time that the CT was ordered and LP performed. Nonetheless, there were undoubted gradients of SAH suspicion that prompted clinicians to further evaluate some patients with angiography.



B.	Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?	No. The gold standard was subarachnoid blood on CT, xanthochromia, > 5 rbc in CSF with angiographic aneurysm, or autopsy. There is no statement of blinding of outcome assessors to other clinical data.																																																
C.	Did the results of the test being evaluated influence the decision to perform the gold standard?	Probably. There were undoubtedly gradients of SAH suspicion that prompted clinicians to further evaluate (LP or angiography) some patients.																																																
II. What are the results?																																																		
A.	What likelihood ratios were associated with the range of possible test results?	<ul style="list-style-type: none"> • 592 patients enrolled including 61 with SAH • Follow-up was achieved in 89.6% (80.4% by telephone, 9.2% by repeat visit to one of the hospitals after enrollment). • Serious headache (SAH, bacterial meningitis, intracerebral hemorrhage, cancer, or ischemic stroke) accounted for 11.7% of headaches – including 61/592 (10.3%) with SAH. • The most common diagnoses were benign headache (46.5%) and migraine (26.4%) • There were no false-positive CT scans so all false-positives were because of > 5 rbc in the final tube of CFS (traumatic LP's). • The authors report the following accuracy for this CT-LP strategy. <table border="0" style="margin-left: 40px;"> <tr><td></td><td colspan="2" style="text-align: center;">SAH</td><td></td></tr> <tr><td></td><td style="text-align: center;">Yes</td><td style="text-align: center;">No</td><td></td></tr> <tr><td>CT* or LP*</td><td style="text-align: center;">61</td><td style="text-align: center;">175</td><td style="text-align: right;">SEN 100 (94-100)</td></tr> <tr><td>CT and LP*</td><td style="text-align: center;">0</td><td style="text-align: center;">356</td><td style="text-align: right;">Spec 67 (63-71)</td></tr> <tr><td></td><td></td><td></td><td style="text-align: right;">LR* 3.0 (2.7-3.5)</td></tr> <tr><td></td><td></td><td></td><td style="text-align: right;">LR* < 0.00001</td></tr> </table> • In a sensitivity analysis, the authors assume that one patient who was lost to follow-up (1/60 = 1.7%) had a SAH (false negative) yielding the following estimates of diagnostic accuracy. <table border="0" style="margin-left: 40px;"> <tr><td></td><td colspan="2" style="text-align: center;">SAH</td><td></td></tr> <tr><td></td><td style="text-align: center;">Yes</td><td style="text-align: center;">No</td><td></td></tr> <tr><td>CT* or LP*</td><td style="text-align: center;">61</td><td style="text-align: center;">175</td><td style="text-align: right;">SEN 98 (91-100)</td></tr> <tr><td>CT and LP*</td><td style="text-align: center;">1</td><td style="text-align: center;">355</td><td style="text-align: right;">Spec 67 (63-71)</td></tr> <tr><td></td><td></td><td></td><td style="text-align: right;">LR* 2.98 (2.6-3.4)</td></tr> <tr><td></td><td></td><td></td><td style="text-align: right;">LR* 0.024 (0.0-0.17)</td></tr> </table> 		SAH				Yes	No		CT* or LP*	61	175	SEN 100 (94-100)	CT and LP*	0	356	Spec 67 (63-71)				LR* 3.0 (2.7-3.5)				LR* < 0.00001		SAH				Yes	No		CT* or LP*	61	175	SEN 98 (91-100)	CT and LP*	1	355	Spec 67 (63-71)				LR* 2.98 (2.6-3.4)				LR* 0.024 (0.0-0.17)
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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?	<p>Uncertain since certain key details of study methodology were omitted (see STARD criteria) including,</p> <ul style="list-style-type: none"> • CT scanner details (first generation scanners?) • Number of and experience of outcome assessors (neuroradiologists reading CT's) • Interval between CT and LP • Exclusion of those who refuse LP? <p>In general, CT scan quality and neuro-radiologist experience in interpreting non contrast head CT's for SAH have only improved so with baseline sensitivity of CT (55/61=90%) and LP expertise/technique essentially unchanged, the estimates of sensitivity would only be expected to improve since 2003 and specificity would be static.</p>
B.	Are the results applicable to the patients in my practice?	No, but this study is practice affirming and begins to provide estimates of diagnostic accuracy and pretest probability by which to estimate test-treatment thresholds (see below).
C.	Will the results change my management strategy?	Yes, if clinicians recognize that the pre-test probability of SAH among those in the ED who we suspect has SAH (before CT or LP) is 10.3%.
D.	Will patients be better off as a result of the test?	<p>Using Pauker's formula at left (see attached spreadsheet calculator) and the conservative (sensitivity analysis derived) estimates of sensitivity and specificity, one gets the following:</p> <p>$P_{pos/nd} = 1 - spec = 0.33$ $P_{neg/nd} = spec = 0.67$ $P_{pos/d} = sen = 0.98$ $P_{neg/d} = 1 - sen = 0.02$</p> <p>Then one needs to ascertain the risk of the test (R^+), benefit of treatment in someone with disease (Brx) and risk of treatment in someone without disease (Rrx). In the era of CT, the risk of post-LP herniation is exceedingly rare. Other complications are not so rare including Post-LP headache (40% - McSwiney 1995, Lybecker 1990, Lybecker 1995), spinal or epidural hematoma (Roos 2003), or backache (35%, Evans 1998). To focus on serious complications of LP</p>



		<p>(headache for up to 1-year, prolonged backache, nerve root injury, or iatrogenic meningitis) we will use the figure of 0.3% (Evans 1998). Hillman et al demonstrated that 72% of past or future patients with early interventions had a good recovery versus 50% of those with delayed surgery. In the absence of an RCT, will use these values to estimate an absolute risk reduction of 22%. The risk of clipping or coiling a cerebral blood vessel that does not have an aneurysm would be in 8% intracranial hemorrhagic complication (Bodily 2011), although for a patient without a cerebral aneurysm to proceed to coiling would require a series of false positives: CT, LP, angiography.</p> <p>Therefore, $R_{rx} = 0.08$, $R^+ = 0.003$, $Br_x = 0.22$ which yields Test Threshold = 0.12 and Treatment Threshold = 0.87.</p>
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Limitations

- 1) Insufficient [detail](#) about CT technology (first generation scanner?) or neuro-radiologist experience.
- 2) Failure to report CSF rbc as [interval likelihood ratios](#).
- 3) Failure to state timing of CT then LP (duration of headache prior to CT, interval between CT and LP).
- 4) Failure to state blinding of outcome assessors to other clinical data.
- 5) 10% lost to follow-up with optimistic sensitivity analysis.

Bottom Line

In ED patients with headache or syncope-associated headache suspicious for SAH, the prevalence (pre-test probability) of SAH is 10%, while the most common alternative diagnoses are benign headache (46.5%) or migraine (26.4%). Although 10% of the current study were lost to follow-up, assuming that 1/60 of those without follow-up had SAH the LR^+ for subarachnoid blood on CT of >5 rbc in last tube of

CSF is 2.98 (95% CI 2.6-3.4) and the LR⁻ is 0.024 (95% CI 0.0-0.17). An abnormal CT or > 5 in CSF_{rbc} would not confirm the diagnosis of SAH (would increase probability for 10% to 25%) but negative results on CT and LP would significantly reduce the probability of SAH from 10% to 0.27% (95% CI 0-1.9%). Further diagnostic research using contemporary CT scanners and explicit descriptors of STARD criteria will further define the diagnostic accuracy of CT and LP. In addition, the diagnostic accuracy of history, physical exam, and physician gestalt should be explored, perhaps in constructing a SAH clinical decision rule.

