Lumbar Puncture After Negative Imaging in Patients With Suspected Subarachnoid Hemorrhage

Opposing authors provide succinct, authoritative discussions of controversial issues in emergency medicine. Authors are provided the opportunity to review and comment on opposing presentations. Each topic is accompanied by an Editor's Note that summarizes important concepts. Participation as at authoritative discussant is by invitation only, but suggestions for topics and potential authors can be submitted to the section editors.

Editor's Note: *The sensitivity of computed tomographic (CT) head imaging in detecting subarachnoid hemorrhage has substantially increased in recent years. As a consequence, very few patients with a negative CT scan result will actually have subarachnoid hemorrhage. Efforts to identify patients with rare subarachnoid hemorrhage will require performing lumber punctures on a large population of disease-free individuals. In this installment of Clinical Controversies, opposing advocates address the issues that arise in subjecting a large population to unpleasant evaluations to detect a dangerous diagnosis in a small minority.*

LUMBAR PUNCTURE IS NECESSARY FOR RULING OUT ATRAUMATIC SUBARACHNOID HEMORRHAGE SIX HOURS AFTER SYMPTOM ONSET

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Subarachnoid hemorrhage is a deadly disease that commonly presents with acute onset of atraumatic headache. Initial misdiagnosis leads to worse outcomes owing to delays in management.[1] High-risk patients with negative computed tomographic (CT) imaging results obtained more than 6 hours from symptom onset should undergo lumbar puncture as opposed to no further evaluation.

Noncontrast CT of the head followed by lumbar puncture if the result is negative is the historical mainstay for the diagnosis of atraumatic subarachnoid hemorrhage. Yet CT sensitivity decreases with time from symptom onset. A prospective cohort study of 3,132 patients reported a sensitivity of 100% within 6 hours of symptom onset but 85.7% thereafter.[2] Meta-analysis data suggest that a negative CT result obtained greater than 6 hours from symptom onset yields a negative likelihood ratio (LR–) of 0.07 for the diagnosis of subarachnoid hemorrhage.[3]

Adding lumbar puncture to CT imaging yields a near 100% sensitivity for the diagnosis of subarachnoid hemorrhage regardless of time elapsed from symptom onset.[4] Estimated lumbar puncture numbers needed to identify actionable cases of subarachnoid hemorrhage are highly situation dependent. Published estimates range from 91 to 15,200.[3] We believe these numbers represent overestimates because they come from studies examining lumbar punctures for any indication or studies excluding patients with features placing them at high risk for subarachnoid hemorrhage. Lumbar puncture offers the most sensitive tool for ruling out subarachnoid hemorrhage and also facilitates the diagnosis of alternative actionable diagnoses such as meningitis.[4]

Lumbar punctures are not without risk. Potential complications include post–lumbar puncture headache, bleeding, and brainstem herniation. That said, the risk of catastrophic complications such as herniation is low, provided clinicians appropriately screen patients for

contraindications such as bleeding diatheses and focal neurologic deficits.[3] Unfortunately, traumatic taps are common, which can erroneously inflate the numbers of RBCs in the cerebrospinal fluid. Because this type of tap occurs in up to 15% of procedures, results can be challenging to interpret when clinicians are trying to avoid false-positive ones.[5] The resultant loss in specificity is the price clinicians pay for the sensitivity offered by this procedure.

Whether a particular patient is more likely to experience benefit versus harm from a lumbar puncture procedure depends entirely on the probability of subarachnoid hemorrhage in that patient. Historical and physical examination features define probability of disease, in turn driving the utility of diagnostic procedures.[3] The Ottawa Subarachnoid Hemorrhage Rule defines characteristics of patients at particularly high risk for subarachnoid hemorrhage: older than 40 years, complaint of neck pain or stiffness, witnessed loss of consciousness, onset with exertion, thunderclap headache, and limited neck flexion on examination.[6,7] Patients at highest risk of subarachnoid hemorrhage are most likely to benefit from lumbar puncture.

To illustrate this point, consider 3 separate patients. First is an intermediate-risk patient whose risk of subarachnoid hemorrhage matches the prevalence identified in a meta-analysis of studies of subarachnoid hemorrhage diagnostic evaluation, 7.5%.[3] Second is a low-risk patient whose headache did not reach maximal intensity within 1 hour, a feature with an LR– of 0.06, yielding a subarachnoid hemorrhage probability of 4.8%. Third is a high-risk patient with neck stiffness on examination, a feature with a positive LR of 6.6, yielding a subarachnoid hemorrhage probability of 34.8%. Given an LR– of 0.07, a negative CT result obtained greater than 6 hours from symptom onset yields a posterior probability of disease of 0.3% for the low-risk patient, 0.6% for the intermediate-risk patient, and 2.3% for the high-risk patient (Figure). Using Pauker's formula for testing threshold,[8] we assume lumbar puncture sensitivity is 100%,[4] specificity is 67%,[4] and risk of mortality approximates 0%. We assume mortality reduction owing to surgical intervention is 14%[1] and periprocedural mortality is 0.7%.[9] This yields a testing threshold of 1.6%. The high-risk patient's posterior probability of

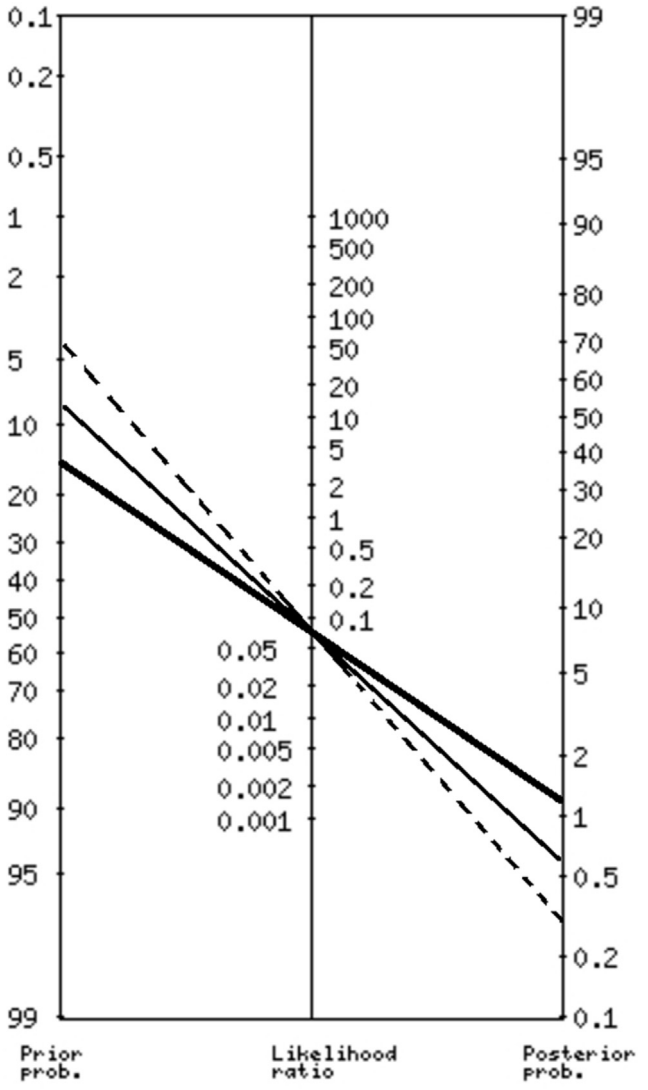

Figure. Fagan nomogram. The left axis represents the pretest probability of subarachnoid hemorrhage. The center axis represents the LR of a negative result for noncontrast CT of the brain obtained greater than 6 hours from symptom onset (0.07). The right axis represents the posttest probability of subarachnoid hemorrhage after the negative CT result. In the case of a low-risk patient with a pretest probability of subarachnoid hemorrhage of 4.8%, the posttest probability of subarachnoid hemorrhage is 0.3% (dashed line). For an intermediate-risk patient with a pretest probability of subarachnoid hemorrhage of 7.5%, posttest subarachnoid hemorrhage probability decreases to 0.6% (solid line). A high-risk patient with a pretest probability of disease of 34.8% still retains a posttest probability of subarachnoid hemorrhage of 2.3% (bold line).

disease exceeds this value; hence, he or she should undergo lumbar puncture. For the other 2 patients, lumbar puncture is likely to do more harm than good.

Clinical reality is that scenarios will arise in which the probability of disease approximates the testing threshold, leading to decisional equipoise. Shared decisionmaking can balance the risks and benefits in determining diagnostic strategy in these patients. Subarachnoid hemorrhage represents a dangerous condition, the presentation of which is often not distinct from that of the high volume of emergency department patients with headache. Hence, the diagnostic evaluation for this condition is not always clear, making it an optimal scenario for use of shared decisionmaking.[10] Yet among high-risk patients with negative-result head CT imaging obtained greater than 6 hours from symptom onset, we believe lumbar puncture must be the default course of action to minimize the risk of a missed subarachnoid hemorrhage diagnosis.

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LUMBAR PUNCTURE SHOULD NOT BE ROUTINELY PERFORMED FOR SUBARACHNOID HEMORRHAGE AFTER A NEGATIVE HEAD CT

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Headache is a common presenting complaint in the emergency department (ED), and approximately 1% of patients with a sudden-onset headache receive a diagnosis of subarachnoid hemorrhage.[1] Historically, it has been taught that a lumbar puncture is required after a negative computed tomographic (CT) result to exclude the diagnosis. However, in light of improving CT quality, the value of this approach has been questioned. In accordance with the current evidence, we argue that lumbar puncture is not routinely required to rule out subarachnoid hemorrhage after a negative head CT scan result, even if the CT was performed more than 6 hours after symptom onset.

The most important argument against lumbar puncture is the accuracy of modern CT scanners. The tradition of performing a lumbar puncture after CT started in an era when CT was more likely to miss a diagnosis of subarachnoid hemorrhage. Using modern CT technology, Perry et al[2] demonstrated 100% sensitivity (95% confidence interval 97% to 100%) of CT within 6 hours for the diagnosis of subarachnoid hemorrhage.[2] Although a CT performed greater than 6 hours after symptom onset is less sensitive, the prevalence of subarachnoid hemorrhage also decreases among patients presenting later.[3] In the original study by Perry et al,[2] there were 2,179 patients

(5.5% overall subarachnoid hemorrhage prevalence) who had CT performed more than 6 hours after symptom onset. Among patients with an initially normal CT result, 17 (0.8%; 95% confidence interval 0.5% to 1.3%) ultimately received a diagnosis of subarachnoid hemorrhage, and only 6 (0.3%) underwent neurosurgical intervention.[2] Therefore, a negative CT result after 6 hours results in a very low posttest probability.

Even a perfect test will struggle to perform when the prevalence of disease is less than 1%, and lumbar puncture is not a perfect test. Sensitivity and specificity vary, depending on whether one is measuring xanthochromia, RBCs, or both, as well as the thresholds used and the timing of the test; however, no combination has both a sensitivity and specificity greater than 90% when accounting for 95% confidence intervals.[1] For example, a lumbar puncture looking for more than $1{,}000\times10^6$ RBCs/L has a sensitivity of approximately 76% and a specificity of approximately 88%.[1] In fact, studies have reported a number needed to test for lumbar punctures of 250 to 15,200 RBCs/L.[1] The matter is further complicated by "traumatic taps," which occur in 10% to 30% of patients, and can render lumbar puncture results uninterpretable.[4] Given that the prevalence of subarachnoid hemorrhage after a negative CT result is less than 1%, a 10% to 30% incidence of traumatic taps means that uninterpretable or false-positive lumbar puncture results will significantly outnumber true-positive ones.

Although the benefits of a lumbar puncture in this low-risk population are questionable, the harms are clear. The procedure is painful and anxiety provoking for most patients. Post–lumbar puncture headaches occur after 4% to 10% of lumbar punctures and can be debilitating.[5] Furthermore, lumbar punctures can cause rare but serious adverse events, including epidural hematomas and infections. Finally, the lumbar puncture takes time and resources, which can result in a delay to diagnosis (compared with immediate CT angiography in a patient at high risk for subarachnoid hemorrhage), prolong patient stays, and divert attention from other critically ill patients in the ED.

Although the lumbar puncture is often referred to as the standard of care, the evidence suggests otherwise. Even in a study environment, in which physicians know their behavior is being monitored, lumbar punctures were performed in only approximately half of all patients and less than 10% of patients who presented more than 6 hours after symptom onset.[2] This suggests physicians are already using clinical judgment to make this decision, rather than simply performing lumbar punctures routinely.

Much like the evaluation of pulmonary embolism, a zero-miss rate may not be possible or even appropriate. The test threshold for lumbar puncture after a negative CT result has been calculated to be approximately 2% to 4%, meaning the harms associated with a lumbar puncture outweigh the benefits in patients with a pretest probability below that threshold.[1,6] Considering that the prevalence of subarachnoid hemorrhage among patients with sudden-onset headache after a negative CT result is less than 1%, this suggests lumbar puncture should not be performed routinely.[2]

Figure. Potential causes of false-negative CT results.[7]

Older-generation CT scanners (second generation or older)
CT uses imaging slices >5 mm when imaging through the base of the brain
Motion artifact
Artifact owing to metal in the surrounding bone or soft tissue
Interpreting radiologist not an attending physician
Hematocrit level <30%

In a patient with a severe headache, premature closure of the differential diagnosis is likely if the physician considers only subarachnoid hemorrhage. A lumbar puncture may still be required to rule out other diagnoses (eg, meningitis, encephalitis), and some patients may be at high enough risk based on clinical features or risk factors for a false-negative CT result (Figure) to consider a lumbar puncture in the evaluation of subarachnoid hemorrhage. However, the risk of subarachnoid hemorrhage after a negative head CT result is very low, even when that CT is performed more than 6 hours after symptom onset. The test threshold calculations indicate the harms will outweigh benefits for the average patient, and therefore lumbar puncture should not be performed routinely. Physician judgment will be required to identify select, high-risk patients who may require further investigation (eg, lumbar puncture, CT angiography, magnetic resonance imaging) after the negative head CT result, and shared decisionmaking using data such as the number needed to test will be necessary to determine whether the next test should be a lumbar puncture or an alternate modality, such as CT angiography.

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