EDITORIAL

High-Stakes Diagnostic Decision Rules for Serious Disorders
The Ottawa Subarachnoid Hemorrhage Rule

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Diagnostic errors lead to death or disability for an estimated 150 000 patients in the United States each year.[1] The emergency department is a known high-risk location for misdiagnosis.[2] Missed ischemic stroke and brain hemorrhage are recognized sources of diagnostic error, with approximately 9% of cerebrovascular events missed at first emergency department contact,[3] including an estimated 20% of subarachnoid hemorrhages in patients presenting with normal mental status.[4] Because effective treatments are available, diagnostic delays increase morbidity and mortality 3- to 8-fold,[4,5] so accurate early diagnosis is important.

Rates of missed subarachnoid hemorrhage in the 1980s and 1990s were estimated at 32%,[6] although more recent estimates suggest the rate is approximately 12%, with about half occurring in the emergency department.[7] Some improvement is probably from newer-generation computed tomography (CT),[7,8] but most is not.[9] The current recommended standard of care is to obtain cranial CT for patients with new, rapid-onset, severe headaches and, for those with nondiagnostic CTs who are still suspected of having possible subarachnoid hemorrhages, to follow with diagnostic lumbar puncture.[10] This "CT-LP" rule is a proven method, with sensitivity for subarachnoid hemorrhage close to 100% when performed correctly.[11] However, because the real-world emergency department miss rate for subarachnoid hemorrhage is approximately 6%,[7] the CT-LP rule either is not applied to all at-risk patients or is used incorrectly (eg, lumbar puncture is obtained too early or too late, when spinal fluid findings may be misleading).

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In this issue of *JAMA*, Perry and colleagues[12] seek to enhance the clinical capabilities for diagnosing subarachnoid hemorrhage through validation and refinement of the Ottawa SAH Rule. The authors present the results of a prospective, cross-sectional study involving 2131 patients with acute headache and demonstrate that their best bedside decision rule identified all cases of subarachnoid hemorrhage (n = 132) among emergency department patients presenting with new, isolated headaches. The final rule relies on the presence of any 1 of 6 findings (age ≥40 years; neck pain or stiffness; witnessed loss of consciousness; onset during exertion; thunderclap headache [instantly peaking pain]; limited neck flexion on examination) and has an estimated sensitivity of 100% for detecting atraumatic subarachnoid hemorrhage. This rule offers the potential to reduce missed subarachnoid hemorrhage and decrease unnecessary, invasive diagnostic testing for patients with low-risk headaches.

Is the Ottawa SAH Rule clinically useful? Any test with near-perfect sensitivity has an intrinsic appeal because a negative result effectively rules out the target disorder. The rule proposed by Perry et al also has a "rule-out power" or negative likelihood ratio (ie, extent to which the odds of having a diagnosis will change following a negative test result) of 0.024, translating to a 42-fold reduction (ie, 1.0/0.024) in the likelihood of subarachnoid hemorrhage. For instance, a patient with acute headache and a pretest probability of 10% who has a negative result with the Ottawa SAH rule would have a posttest probability of 0.3% (ie, convert pretest probability [10%] to pretest odds [1:9]; multiply by 0.024 to obtain posttest odds [0.024:9]; then convert back to probability: 0.024/[0.024 + 9] = 0.00266 = 0.3%. For clinicians uncomfortable converting probability to odds and back, pocket-card nomograms provide a simple graphical interpretation of pretest and posttest probabilities using likelihood ratios). This is a clinically useful result because "very low" residual risks (<1%) of dangerous disorders may be considered acceptable in the emergency department,[13] particularly when shared decision-making approaches that consider patient preferences (eg, whether a patient prefers the small residual risk of missed subarachnoid hemorrhage or the risks of a false-positive lumbar puncture following a traumatic tap, including follow-up angiography) are used effectively.[14]

However, there are several important caveats for application of this decision rule. Effective use of any decision rule requires careful attention to clinical details affecting its generalizability. Does the patient meet all original inclusion criteria, such as having a headache that peaked in less than an hour? Has an examination been performed carefully enough to verify that neurologic status is truly normal, including no papilledema? Is subarachnoid hemorrhage the only target diagnosis being considered, or are unstudied, rare, yet important causes of sudden-onset headache (eg, cerebral venous sinus thrombosis, pituitary apoplexy, arterial dissection) still part of the differential diagnosis? Are other unstudied variables (eg, family history of brain aneurysms) present that might complicate interpretation of the rule?

In clinical practice, "rules creep" can lead to overly broad application of a decision rule. Such creep in the setting of headache could be toward patients who present with severe headaches that are more gradual in onset. This misuse could present a problem for patients, especially if the rule were used to

exclude causes other than subarachnoid hemorrhage. Dangerous causes of headache other than subarachnoid hemorrhage were mostly identified by the rule in the sample studied by Perry et al (n = 50/54 [93%]).[12] However, this may not hold true for similar dangerous causes in patients with new headaches that are more gradual in onset (ie, developing over hours to days, rather than seconds to minutes). Medical emergencies such as obstructive hydrocephalus, giant cell arteritis, bacterial brain abscess, and fungal meningitis can present with more gradual-onset headaches without focal neurologic or other red-flag features.[15]

If used in the correct patients, will the new decision rule help reduce missed subarachnoid hemorrhages? To reduce missed cases, the approach would need to outperform current real-world practice and be used more often than the CT-LP rule. This seems plausible, because the sensitivity of the rule is estimated at 100% (lower 95% confidence limit, 97.2%), and this approach is less invasive than CT-LP. However, any reduction in missed cases assumes that accuracy estimates are correct (the final rule still lacks full, prospective validation) and the rule is correctly and consistently applied. This latter point is critical—similarly simple-sounding decision rules are interpreted incorrectly for up to one-third of patients.[16] Because some aspects of the rule depend on subjective physician interpretation (eg, headache peaking "instantly"), subtle physician biases (eg, linked to physician risk tolerance[17]) might lead to underuse or overuse of imaging unrelated to true disease risk.

If applied correctly, will the Ottawa SAH Rule help reduce unnecessary diagnostic workups? Theoretically the rule might reduce use of CT, but the specificity of the rule is low (15.3%). In the study by Perry et al, imaging could have been avoided in only 305 of the 2131 patients (14%).[12] Further, emergency department clinicians must be willing to discharge a patient with new headache based on history and examination alone. This possibility is made less likely given that the rule misses some dangerous causes of headache, which clinicians must rule out separately on their own. Reducing lumbar punctures would seem a more realistic goal, although not all at-risk patients receive an appropriate lumbar puncture in current practice, so the number of procedures avoided will likely be small. Even if lumbar punctures are reduced, the overall cost-effectiveness of diagnostic workups for subarachnoid hemorrhage might not increase much.[18]

How should clinicians use this decision rule? Because the adverse consequences of missing a well-appearing patient with an aneurysmal subarachnoid hemorrhage are great,[4] clinicians will understandably need to be highly confident that subarachnoid hemorrhage has been excluded for the individual patient they are evaluating. Recognizing imprecision in study results based on sampling error, a conservative physician might evaluate the present study's findings using the "worst reasonable" expected performance of the rule's utility (ie, 95% confidence bound). The more conservative 95% confidence limit on the Ottawa SAH Rule's negative likelihood ratio is 0.39 (Table 3 in Perry et al).[12] If this were the true value (instead of 0.024), it would effectively nullify the utility of the rule—ie, a negative result would decrease pretest probabilities of subarachnoid hemorrhage from 5%, 10%, and 20% to just 2.0%, 4.2%, and 8.9%, respectively. Applying the rule after CT but before lumbar puncture is a possible option to hedge against rule imprecision, but data supporting this approach leave similar levels of uncertainty (89% sensitivity at the lower 95% confidence limit)[8] for scientifically conservative clinicians.

These facts raise important general questions about development and use of clinical decision rules to exclude uncommon, lethal disorders. These high-stakes scenarios require both a highly accurate rule and an ineffective, risky, or cumbersome diagnostic alternative. This concept, based on net health value (balancing benefits and risks) relative to the alternative of pursuing additional testing,[19] differs from the more common but less helpful notion of seeking a "safe discharge."[20] Despite the high sensitivity of the Ottawa SAH Rule, these conditions are probably not met, because CT-LP has relatively low risk and only modest inconvenience. It is possible the Ottawa SAH Rule may have greater utility in situations, although uncommon, in which the CT-LP combination is not readily available or cannot easily be applied.

Research in this area is hampered by trade-offs inherent in diagnosis of uncommon, dangerous disorders. Studying higher-risk populations enriches the sample with the target disorder, increasing precision but limiting generalizability and risking low utility if pretest probabilities are too high (making workups inevitable). Conversely, studying lower-risk populations dilutes the target disorder in the sample, increasing generalizability but reducing precision and risking low utility if pretest probabilities are too low (making workups futile); doing so can also make the research prohibitively expensive. Guidelines for diagnostic decision rule development should be adapted to include rules seeking to identify high-stakes, dangerous disorders. This may mean prespecifying thresholds for pretest probability above and below which diagnostic rules would not improve patient care.

Future studies should seek to validate the Ottawa SAH Rule using larger samples. Realistically, though, this may require use of administrative data and imputation of missing results.[8] The rule should also be studied for the effect on patient outcomes as part of a clinical care pathway for headache diagnosis, ideally with direct comparison to an alternate care pathway based on the CT-LP rule. While awaiting further scientific advances, clinicians may find the refined Ottawa SAH Rule helpful to guide diagnostic decisions, but they should limit its use to patients with acute headache who are similar to those among whom the rule has been evaluated.

ARTICLE INFORMATION

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