Original Investigation

Clinical Decision Rules to Rule Out Subarachnoid Hemorrhage for Acute Headache

Jeffrey J. Perry, MD, MSc; Ian G. Stiell, MD, MSc; Marco L. A. Sivilotti, MD, MSc; Michael J. Bullard, MD; Corinne M. Hohl, MD, MHSc; Jane Sutherland, MEd; Marcel Émond, MD, MSc; Andrew Worster, MD; Jacques S. Lee, MD, MSc; Duncan Mackey, MD; Merril Pauls, MD; Howard Lesiuk, MD; Cheryl Symington, RN, ENCC; George A. Wells, PhD

Editorial page 1237

IMPORTANCE Three clinical decision rules were previously derived to identify patients with headache requiring investigations to rule out subarachnoid hemorrhage.

OBJECTIVE To assess the accuracy, reliability, acceptability, and potential refinement (ie, to improve sensitivity or specificity) of these rules in a new cohort of patients with headache.

DESIGN, SETTING, AND PATIENTS Multicenter cohort study conducted at 10 university-affiliated Canadian tertiary care emergency departments from April 2006 to July 2010. Enrolled patients were 2131 adults with a headache peaking within 1 hour and no neurologic deficits. Physicians completed data forms after assessing eligible patients prior to investigations.

MAIN OUTCOMES AND MEASURES Subarachnoid hemorrhage, defined as (1) subarachnoid blood on computed tomography scan; (2) xanthochromia in cerebrospinal fluid; or (3) red blood cells in the final tube of cerebrospinal fluid, with positive angiography findings.

RESULTS Of the 2131 enrolled patients, 132 (6.2%) had subarachnoid hemorrhage. The decision rule including any of age 40 years or older, neck pain or stiffness, witnessed loss of consciousness, or onset during exertion had 98.5% (95% CI, 94.6%-99.6%) sensitivity and 27.5% (95% CI, 25.6%-29.5%) specificity for subarachnoid hemorrhage. Adding "thunderclap headache" (ie, instantly peaking pain) and "limited neck flexion on examination" resulted in the Ottawa SAH Rule, with 100% (95% CI, 97.2%-100.0%) sensitivity and 15.3% (95% CI, 13.8%-16.9%) specificity.

CONCLUSIONS AND RELEVANCE Among patients presenting to the emergency department with acute nontraumatic headache that reached maximal intensity within 1 hour and who had normal neurologic examination findings, the Ottawa SAH Rule was highly sensitive for identifying subarachnoid hemorrhage. These findings apply only to patients with these specific clinical characteristics and require additional evaluation in implementation studies before the rule is applied in routine clinical care.

JAMA. 2013;310(12):1248-1255. doi:10.1001/jama.2013.278018

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Jeffrey J. Perry, MD, MSc, Clinical Epidemiology Unit, F647, Ottawa Hospital, 1053 Carling Ave, Ottawa, Ontario, Canada K1Y 4E9 (jperry@ohri.ca).

Investigation of the neurologically intact (ie, no neurologic deficits) patient with headache is a potentially difficult clinical decision for physicians. Headache accounts for approximately 2% of all emergency department visits, and subarachnoid hemorrhage is one of the most serious diagnoses, accounting for only 1% to 3% of these headaches.[1-4] Although the decision to evaluate patients with new neurologic deficits is relatively straightforward, it is much more difficult to determine which alert, neurologically intact patients who present with headache alone require investigations—yet such patients account for half of all subarachnoid hemorrhages at initial presentation.[5] This diagnostic dilemma is illustrated by the report that 5.4% of confirmed subarachnoid hemorrhages were misdiagnosed during the patients' initial emergency department assessment.[6]

Patients suspected of having subarachnoid hemorrhage are typically evaluated with an unenhanced computed tomography (CT) scan followed by a lumbar puncture if results of the CT scan are negative. Computed tomography is highly sensitive when performed soon after headache onset.[7] Lumbar puncture can be a painful procedure and can result in a headache that may be worse than the original headache.[8]

A clinical decision rule is derived from original research and is defined as a decision-making tool that incorporates 3 or more variables from the history, examination, or simple tests.[9-12] These rules help clinicians with diagnostic or thera-

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

peutic decisions at the bedside. Three clinical decision rules, each containing 4 clinical variables, had been prospectively derived in a previous separate cohort of 1999 patients with headache to determine which patients require investigation for subarachnoid hemorrhage.[13]

The objectives of this study were to prospectively assess the accuracy, reliability, clinical acceptability, potential for rule refinement, and potential effect of these 3 candidate rules in a new cohort of neurologically intact patients with acute headache. Prospective validation of a clinical decision rule is optimally done prior to its use for patient care.[9-12]

Methods

Study Population

This prospective multicenter cohort study was conducted in the emergency departments of 10 university-affiliated urban Canadian tertiary care teaching hospitals from April 2006 to July 2010. These hospitals included 4 of the 6 tertiary care centers that participated in the previous derivation study and 6 new sites.[13] Consecutive adult patients (defined as patients 16 years or older) whose chief reason for visiting the emergency department was a nontraumatic headache that reached maximal intensity within 1 hour were considered for enrollment. We enrolled patients who had a Glasgow Coma Scale score of 15 of 15 (ie, alert and oriented), had not sustained a fall or direct head trauma in the previous 7 days, and who had presented within 14 days of headache onset.[14]

Patients were ineligible if they had a history of 3 or more recurrent headaches of the same character and intensity as the presenting headache over a period greater than 6 months (ie, established recurrent headache syndromes); were referred from another hospital with a confirmed subarachnoid hemorrhage; returned for reassessment of the same headache if already investigated with both CT and lumbar puncture; had papilledema on fundoscopic examination (as determined by the treating physician); had new focal neurologic deficits (eg, isolated cranial nerve palsies, limb weakness); or had a previous diagnosis of cerebral aneurysm, subarachnoid hemorrhage, brain neoplasm, or hydrocephalus. The research ethics board at each participating center approved the study without the need for written consent. Participants were informed that they might be contacted by telephone for follow-up, and verbal consent was obtained from such patients at the time of telephone contact.

Assessments

All patient assessments were made by attending physicians certified in emergency medicine or emergency medicine residents supervised by staff physicians. Physicians were oriented to the study and the standardized assessment by means of a formal 1-hour teaching presentation. After assessing patients, but before ordering imaging or cerebrospinal fluid analysis, physicians were instructed to record 19 clinical findings on data forms (these were variables either found to be significant in the previous derivation study or felt to be possibly clinically important for potential rule refinement). To assess sensibility, physicians answered 2 questions related to interpretation and use of each of the 3 proposed "SAH (subarachnoid hemorrhage) Rules": (1) Are investigations indicated for this patient according to the decision rule? (Yes/No); and (2) How comfortable would you be in actually using the rule for this patient? (5-point scale from "very comfortable" to "very uncomfortable").

When feasible (ie, a second physician on duty was able to take the time to conduct a second assessment), some patients were assessed independently by a second physician to measure interobserver agreement. We trained study nurses at each site, by means of a full-day orientation and ongoing monthly feedback from the central study coordinator, to collect data forms, verify data, confirm eligibility, and perform telephone follow-up at 1 and 6 months when necessary. Study nurses also reviewed all emergency department visits to identify any missed patients. If patients with headache were not clearly excluded by the eligibility criteria, they were deemed to be "missed potentially eligible." Information including age, sex, arrival by ambulance, CT, lumbar puncture, and diagnosis of subarachnoid hemorrhage was recorded on a standardized "missed potentially eligible" data collection form. Data were reviewed again centrally by a trained study nurse coordinator who had participated in the previous derivation study.

Outcome Measures

The primary outcome, subarachnoid hemorrhage, was defined by any 1 of the following: subarachnoid blood on unenhanced CT of the head; xanthochromia in the cerebrospinal fluid; or red blood cells (>1×10^6/L) in the final tube of cerebrospinal fluid, with an aneurysm or arteriovenous malformation on cerebral angiography. This outcome was established a priori by consensus of 5 emergency physicians and 1 neurosurgeon.[15]

Patients underwent evaluation with nonenhanced CT scans, lumbar puncture, or both, with cerebrospinal fluid analysis according to the judgment of the treating physician. Physicians were instructed not to alter their practice according to the proposed rules. Computed tomography scans were interpreted by staff radiologists provided with routine clinical information but with not the contents of the data collection forms. Radiologists provided a final radiology report following the scan. Lumbar punctures were performed by the treating physicians, with the laboratory technicians assessing the cerebrospinal fluid for the presence of red blood cells or xanthochromia as determined by visual inspection.[15-18]

We could not require all patients to undergo CT and lumbar puncture, given that practice at the study sites indicated only 80% of eligible patients underwent CT and about 45% underwent lumbar puncture with cerebrospinal fluid analysis.[13] Therefore, patients discharged without both CT imaging and normal lumbar puncture findings (or without both CT imaging and lumbar puncture performed) were evaluated using our Proxy Outcome Assessment Tool. This assessment tool included a structured telephone interview at 1 month and 6 months after emergency department assessment as well as a medical records review to identify any patients who developed a subsequent subarachnoid hemorrhage. The tele-

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

Box 1. Variables Included in Each of the 3 Proposed Rules

Rule 1
Investigate if ≥1 high-risk findings present:
1. Age ≥40 y
2. Neck pain or stiffness
3. Witnessed loss of consciousness
4. Onset during exertion

Rule 2
Investigate if ≥1 high-risk findings present:
1. Age ≥45 y
2. Arrival by ambulance
3. Vomiting (≥1 episodes)
4. Diastolic blood pressure ≥100 mm Hg

Rule 3
Investigate if ≥1 high-risk findings present:
1. Age 45-55 y
2. Neck pain or stiffness
3. Arrival by ambulance
4. Systolic blood pressure ≥160 mm Hg

phone call assessed repeat physician visits, change in diagnosis, and subsequent testing with CT, lumbar puncture, angiography, or magnetic resonance imaging. We internally validated our follow-up tool to identify subarachnoid hemorrhage during our previous phase 1 derivation study.[13] For patients without telephone follow-up or subsequent hospital encounters at the enrolling site, records from the provincial coroner's office, when available, were further checked to identify any deaths compatible with subarachnoid hemorrhage. Patients found to have a subsequent subarachnoid hemorrhage within the following 6 months were classified as positive for events for the enrolling visit, with all others classified as negative.

Statistical Analysis

We assessed the 3 candidate rules (**Box 1**) for their sensitivity and specificity, including 95% CIs, for classifying patients according to whether they had a subarachnoid hemorrhage. Interobserver agreement for each variable and each of the rules as a whole was measured using the κ coefficient. Univariate analysis used a 2-sided *t* test for continuous variables and the Pearson χ^2 test for categorical variables. Potential refinement of the rules was assessed using multivariate recursive partitioning analysis. The estimated sensitivity, specificity, and C statistic for subarachnoid hemorrhage, including 95% CIs, were calculated for the refined rule. We estimated that the required sensitivity needs to be close to 100% to be clinically acceptable. It was determined therefore that we estimated a 100% sensitivity with 95% confidence bands of 97%-100%. Given a prevalence of 6.5% in our previous derivation study, we estimated a sample size of 2000 patients with headache, including 120 with subarachnoid hemorrhage. This would provide a sufficient number of cases to yield the required precision (ie, 95% confidence bands of 97%-100%) of the estimated sensitivity of each rule. Descriptive statistics describing physicians' theoretical comfort using the rules were calculated.

We conducted a post hoc bootstrapping analysis of 1000 iterations to determine the internal stability of the refined Ottawa SAH Rule using our previous derivation cohort (N = 1999). In addition, the sensitivity and specificity were calculated when combining the previous derivation cohort to this present new validation cohort of patients with acute headache. The derivation cohort collected presence of neck stiffness on examination and time from onset to peak headache as variables. A time of 1 second or less was used to indicate a thunderclap headache because an explicit variable called "thunderclap headache" was not contained in the derivation cohort. Analyses were performed using SAS version 9.2 (SAS Institute Inc).

Results

Sites enrolled patients for variable periods from April 2006 to July 2010. The combined average annual census for all sites was 510 000 visits with more than 210 staff physicians. In this study, we enrolled 2131 of 2736 potentially eligible patients (77.9%) (mean age, 44.1 years; women, 1290 [60.5%]; arrived by ambulance, 559 [26.2%]; CT scan obtained, 1767 [82.9%]; lumbar puncture performed, 833 [39.1%]; subarachnoid hemorrhage, 132 [6.2%]). An additional 605 patients (22.1%) were deemed "missed potentially eligible" (**Figure**, **Table 1**). Thirty-five patients (1.6%) without both normal CT and cerebrospinal fluid findings required follow-up; we could not contact these patients by telephone or find evidence that there was subsequent hospital follow-up without evidence of a subarachnoid hemorrhage. None of these patients were seen at their regional neurosurgical center or were identified as dead by the provincial coroner's office. Sixty patients (2.8%) underwent independent assessment by 2 physicians to assess interobserver agreement.

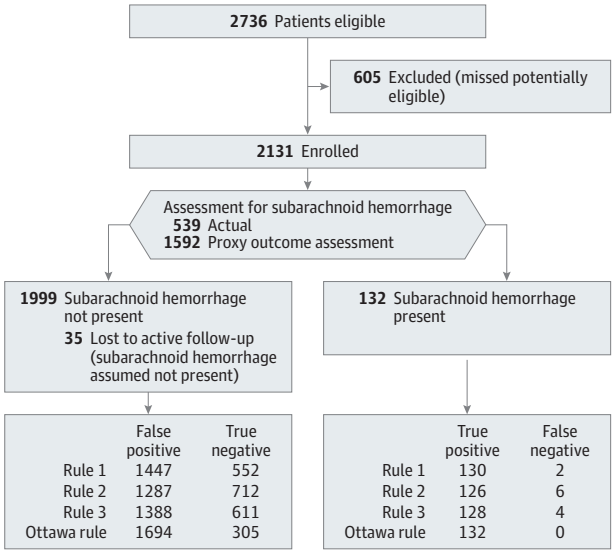
Table 1 reports the characteristics of the enrolled patients, including 132 (6.2%) with subarachnoid hemorrhages. The characteristics of the missed potentially eligible patients were very similar to those of enrolled patients (mean age, 46.0 years; women, 345 [57.0%]; arrived by ambulance, 173 [28.6%]; CT scan obtained, 503 [83.1%]; lumbar puncture performed, 227 [37.5%]; subarachnoid hemorrhage, 33 [5.5%]). Assessments were conducted by staff physicians in 92.7% of enrolled patients.

Table 2 reports the univariate and κ analysis. Patients with subarachnoid hemorrhage were older and had more rapid peaking headaches, onset during exertion, loss of consciousness, neck pain or stiffness, and vomiting; they also more frequently arrived by ambulance and reported experiencing the worst headache of their lives (although this is also commonly reported by patients with benign headaches). Examinations of these patients revealed an elevated blood pressure and limited neck flexion. All of these variables had κ statistics demonstrating moderate (0.40-0.60) to substantial (>0.60) agreement.

The accuracy of the 3 rules is compared in **Table 3**. The sensitivities were 98.5% (95% CI, 94.6%-99.6%) for rule 1, 95.5% (95% CI, 90.4%-97.9%) for rule 2, and 97.0% (95% CI, 92.5%-98.8%) for rule 3. The specificities were 27.6% (95% CI, 25.7%-

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

Figure. Study Flow



29.6%) for rule 1, 30.6% (95% CI, 28.6%-32.6%) for rule 2, and 35.6% (95% CI, 33.6%-37.7%) for rule 3. The κ value for interobserver agreement in the interpretation of the overall rules in 60 cases was 0.86 (95% CI, 0.70-1.0) for rule 1, 0.96 (95% CI, 0.89-1.0) for rule 2, and 0.79 (95% CI, 0.62-0.96) for rule 3. A value greater than 0.60 is generally considered to indicate substantial interobserver agreement.[19]

We refined the rules following additional recursive partitioning analysis, which found that the best model to predict all cases of subarachnoid hemorrhage retained all of the variables in rule 1 plus included the variables "thunderclap headache" (defined as instantly peaking pain) and limited neck flexion on examination (defined as inability to touch chin to chest or raise the head 8 cm off the bed if supine), resulting in a sensitivity of 100% (95% CI, 97.2%-100.0%), specificity of 15.3% (95% CI, 13.8%-16.9%), and C statistic of 0.60 (95% CI, 0.59-0.61). We designated this refined rule the Ottawa SAH Rule (**Box 2**). Our bootstrap analysis (1000 replications) for the Ottawa SAH Rule using the previous phase 1 derivation data set had a sensitivity of 100% (95% CI, 100%-100%) and a specificity of 20.6% (95% CI, 20.5%-20.6%). When the patients in the new validation cohort were combined with those in the previous derivation cohort (N = 4130), the sensitivity for subarachnoid hemorrhage was 100% (95% CI, 98.6%-100%) and the specificity was 17.8% (95% CI, 16.6%-19.1%).

Table 4 reports the characteristics of patients with subarachnoid hemorrhage who were not identified by 1 (or more) of the candidate decision rules. No patient with subarachnoid hemorrhage was missed by all 3 rules. Rule 1 missed 2 cases of subarachnoid hemorrhage. One patient had a nonaneurysmal subarachnoid hemorrhage 6 days after a planned cesarean delivery and had a good outcome without hospitalization or surgical intervention. A CT scan performed on this patient's initial visit demonstrated a small subarachnoid hemorrhage in the frontal sulcus. The patient was assessed by a neurosurgeon, who performed a CT angiogram (the findings of which were normal) and then discharged the patient home from the emergency department. This patient returned 3 days later with another headache, at which time a repeat CT scan also revealed normal findings; the patient

Table 1. Characteristics of Enrolled Patients (N=2131)

Characteristics	Patients, No. (%)
Age, mean (SD) [range]	44.1 (17.1) [15-97]
Women	1290 (60.5)
Arrived by ambulance	559 (26.2)
Time from onset to peak, mean (IQR), s	60 (1-600)
Pain severity at peak (scale, 0-10), mean (SD)	8.7 (1.7)
Onset during exertion	230 (10.8)
Onset during sexual activity	136 (6.4)
Headache awoke patient from sleep	361 (16.9)
Thunderclap headache (ie, instantly peaking pain)	1138 (53.4)
Reported worst headache of life	1600 (75.1)
Loss of consciousness	120 (5.6)
Witnessed	79 (3.7)
Neck pain or stiffness	731 (34.3)
Vomiting	614 (28.8)
Limited flexion on examination	93 (4.4)
Heart rate, mean (SD), beats/min	79.9 (15.6)
Blood pressure, mm Hg	
Systolic	141.4 (23.3)
Diastolic	82.5 (13.7)
Diagnostic procedures and disposition[a]	
CT	1767 (82.9)
Lumbar puncture	833 (39.1)
CT or lumbar puncture	1793 (84.1)
Both CT and lumbar puncture	807 (37.9)
Neither CT nor lumbar puncture	338 (15.9)
Cerebral angiogram performed[b]	321 (15.1)
Admitted to hospital	188 (8.8)
Final diagnosis	
Benign headache	1229 (57.7)
Migraine headache	383 (18.0)
Other benign cause[c]	173 (8.1)
Subarachnoid hemorrhage	132 (6.2)
Viral illness	63 (3.0)
Postcoital headache	39 (1.8)
Ischemic stroke or transient ischemic attack	35 (1.6)
Sinusitis	28 (1.3)
Vasovagal syncope	20 (0.9)
Neck strain	10 (0.5)
Intracerebral hemorrhage	7 (0.3)
Subdural hematoma	6 (0.3)
Brain tumor	4 (0.2)
Bacterial meningitis	2 (0.1)

Abbreviations: CT, computed tomography; interquartile range.

[a] Patients discharged without both CT imaging and normal lumbar puncture findings (or without both CT imaging and lumbar puncture performed) were evaluated using the Proxy Outcome Assessment Tool.

[b] Computed tomography angiography, magnetic resonance angiography, or digital subtraction cerebral angiography.

[c] None of the diagnoses in this category were clinically worrisome for morbidity or mortality.

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

did well subsequently. A second patient had an aneurysm visible on plain CT, without evidence of blood, 1 day following the sudden onset of severe headache. This patient was transferred to the neurosurgical center, where her condition suddenly deteriorated; a repeat CT san revealed a subarachnoid hemorrhage. The aneurysm was treated with intra-arterial coil placement and the patient has done well since, except for some mild unilateral arm weakness. Rule 2 missed 6 patients, 3 of whom required a surgical intervention for aneurysm; rule 3 missed 4 patients, 3 of whom required an intervention for an aneurysm.

Table 2. Interobserver Agreement and Univariate Correlation of Variables for Subarachnoid Hemorrhage

Characteristic	Subarachnoid Hemorrhage, No. (%)		P Value	κ (n = 60)
	No (n = 1999)	Yes (n = 132)		
From history				
Age, mean (SD)	43.6 (17.1)	52.6 (13.6)	<.001	NA
Women	60.7	58.3	.59	NA
Arrived by ambulance	23.9	61.4	<.001	NA
Time from onset to peak, mean (IQR), s	60 (1-600)	10 (1-80)	.002	0.64[a]
Pain severity at peak (scale, 0-10), mean (SD)	8.7 (1.7)	9.5 (1.1)	<.001	0.63[a]
Onset during exertion	10.3	19.2	.002	0.63
Onset during sexual activity	6.2	9.8	.10	0.93
Headache awoke patient from sleep	17.4	12.1	.12	0.77
Thunderclap headache (ie, instantly peaking pain)	54.7	82.4	<.001	0.49
Reported worst headache of life	75.6	99.2	<.001	0.64
Loss of consciousness	5.3	10.6	.01	0.82
Witnessed	3.6	5.3	.32	1.0
Neck pain or stiffness	31.6	76.5	<.001	0.55
Vomiting	26.4	65.9	<.001	0.79
Able to walk since headache started	90.1	76.6	<.001	0.66
Emergency department transfer	8.1	16.7	.001	NA
From physical examination				
Limited flexion	3.2	28.3	<.001	0.44
Heart rate, mean (SD), beats/min	80.2 (15.7)	76.2 (14.0)	.004	NA
Blood pressure, mm Hg				
Systolic	140.7 (23.0)	152.1 (25.6)	<.001	NA
Diastolic	82.3 (13.6)	85.7 (15.2)	.005	NA
Temperature, mean (SD), °C	36.5 (0.65)	36.4 (0.79)	.04	NA
CT obtained	1635 (81.8)	132 (100)	<.001	NA
Lumbar puncture performed	810 (40.6)	22 (16.7)	<.001	NA

Abbreviations: CT, computed tomography; IQR, interquartile range; NA, not applicable.

[a] Spearman interclass correlation coefficient.

Table 3. Sensitivity, Specificity, and Negative Predictive Value of the Original Derived Rules and the Ottawa SAH Rule for Subarachnoid Hemorrhage

Result of Assessment	Rule			
	1	2	3	Ottawa SAH
Positive, No.				
SAH	130	126	128	132
No SAH	1447	1287	1388	1694
Negative, No.				
SAH	2	6	4	0
No SAH	552	712	611	305
Sensitivity, %	98.5 (94.6-99.6)	95.5 (90.4-97.9)	97.0 (92.5-98.8)	100.0 (97.2-100.0)
Specificity, %	27.6 (25.7-29.6)	30.6 (28.6-32.6)	35.6 (33.6-37.7)	15.3 (13.8-16.9)
Negative predictive value, %	99.6	99.0	99.4	100.0
Interobserver agreement, κ (95% CI)	0.86 (0.70-1.0)	0.96 (0.89-1.0)	0.79 (0.62-0.96)	
Likelihood ratio (95% CI)				
Positive	1.36 (1.31-1.40)	1.48 (1.41-1.55)	1.39 (1.33-1.45)	1.17 (1.15-1.20)
Negative	0.054 (0.013-0.21)	0.127 (0.058-0.27)	0.099 (0.037-0.26)	0.024 (0.001-0.39)

Abbreviation: SAH, subarachnoid hemorrhage.

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

We assessed clinical acceptability in 2 ways. Treating physicians indicated their level of comfort in applying and relying on the results of the rule using a 5-point Likert scale, the values of which ranged from "very uncomfortable" to "very comfortable." This comfort was indicated prior to investigating patients. Physicians were "uncomfortable" or "very uncomfortable" using the rules in 18.2% of patients for rule 1, 23.7% for rule 2, and 23.6% for rule 3. The accuracy of physicians' interpretations of the 3 rules was assessed vs the criterion assessment of the standardized coordinating center assessment. Physicians misinterpreted the clinical decision rule as not requiring investigation in 4.7% of patients using rule 1 (theoretically, this could have led to 1 missed subarachnoid hemorrhage), in 6.0% of patients using rule 2 (no subarachnoid hemorrhages), and in 4.6% of patients using rule 3 (including 1 subarachnoid hemorrhage).The most frequently misinterpreted variables were neck pain or stiffness for rules 1 and 3 and arrival by ambulance for rule 2.

The potential influence on clinical practice of applying these rules was assessed vs actual clinical practice. The baseline rate of investigation (CT, lumbar puncture, or both) in this cohort was 84.3%. Rule 1 would have decreased this investigation rate to 74.0%, vs 71.0% for rule 2 and 66.4% for rule 3. The proposed Ottawa SAH Rule would have an investigation rate of 85.7%.

Discussion

In this validation study of clinical decision rules for patients with acute headache, we found our previous rule 1 was highly sensitive for identifying subarachnoid hemorrhage, identifying 130 of 132 cases. If the results of the previous derivation and this current validation study were combined, this rule would identify 260 of 262 subarachnoid hemorrhages, with only 1 patient not identified by this rule undergoing an intervention (the other subarachnoid hemorrhage did not require any intervention). This corresponds to an overall sensitivity of 99.2% (95% CI, 97.3%-99.8%) and specificity of 99.6% (95% CI, 97.9%-99.9%) for subarachnoid hemorrhages undergoing neurologic intervention. Following this rule would decrease the investigation rate to 74.0% from the current investigation rate of 84.1%. While this rule will be acceptable in many practice settings, we further refined the rule to create the Ottawa SAH Rule, which achieved 100% sensitivity. Although aiming for near-perfect sensitivity may lead to fewer missed cases, the trade-off is loss of specificity, increased testing, and increased associated costs. This also translates into a lower C statistic by sacrificing specificity for a highly sensitive rule. This rule may help to standardize which patients with acute headache require investigations and may provide evidence for physicians to use in deciding which patients require imaging to decrease the relatively high rate of missed subarachnoid hemorrhages.[6]

Overall, the sensitivity of each rule is higher than current practice, where it has been estimated that the diagnosis is missed on first visit in at least 5% of patients with subarachnoid hemorrhage.[6] Although emergency physicians have reported that a rule with 99% sensitivity is acceptable, we suspect that the point estimate of 100% for the Ottawa SAH Rule might have greater clinical acceptance than a rule with lower sensitivity.[20] The Ottawa SAH Rule does not lead to a reduction of testing (ie, CT, lumbar puncture, or both) vs current practice; however, it may help to standardize which patients with acute headache require investigations, and its widespread use could help decrease missed subarachnoid hemorrhages.

Box 2. The Ottawa SAH Rule

For alert patients older than 15 y with new severe nontraumatic headache reaching maximum intensity within 1 h

Not for patients with new neurologic deficits, previous aneurysms, SAH, brain tumors, or history of recurrent headaches (≥3 episodes over the course of ≥6 mo)

Investigate if ≥1 high-risk variables present:
1. Age ≥40 y
2. Neck pain or stiffness
3. Witnessed loss of consciousness
4. Onset during exertion
5. Thunderclap headache (instantly peaking pain)
6. Limited neck flexion on examination

SAH indicates subarachnoid hemorrhage.

Table 4. Characteristics of Patients Not Identified by 1 or More Clinical Decision Rules (n = 11)

		Rule						
Age	Sex	1	2	3	Diagnosis	Admitted	Aneurysm	Surgical Intervention
30	Female	Missed	Missed	Identified	Aneurysm	Yes	Yes	Intra-arterial coil
30	Female	Missed	Identified	Identified	Nonaneurysmal	No	No	No
43	Male	Identified	Missed	Identified	Aneurysm	Yes	Yes	Intra-arterial coil
40	Female	Identified	Identified	Missed	Aneurysm	Yes	Yes	Intra-arterial coil
29	Male	Identified	Missed	Identified	False positive	No	No	No
76	Male	Identified	Identified	Missed	Meningioma	Yes	No	Yes for meningioma
61	Female	Identified	Identified	Missed	Aneurysm	Yes	Yes	Intra-arterial coil
69	Male	Identified	Identified	Missed	Aneurysm	Yes	Yes	Clipping
43	Male	Identified	Missed	Identified	Nonaneurysmal	Yes	No	No
39	Female	Identified	Missed	Identified	Aneurismal	Yes	Yes	Clipping
38	Female	Identified	Missed	Identified	Perimesencephalic	Yes	No	No

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

A total of 54 patients enrolled in this study had serious conditions other than subarachnoid hemorrhage (subdural or intracerebral hemorrhages, meningitis, tumor, ischemia). All but 4 of these serious diagnoses (1 ischemic stroke, 1 meningitis, 2 tumors) were in the high-risk classification. It was clear from the medical records that the treating physicians were concerned about the possibility of other pathology. Given the heterogeneity of headache, it is impractical to generate a single clinical decision rule for all causes of headache. In general, most other causes of serious headache have other clinical clues (eg, fever or transient or persistent neurologic deficits) to help guide investigations for other significant pathology. Although the Ottawa SAH Rule should identify most of these other serious diagnoses, patients considered as possibly having these other diagnoses should be investigated appropriately.

This prospective validation study was designed and conducted according to the strict methodological standards for development of clinical decision rules.[9-12] The outcome, subarachnoid hemorrhage, was carefully defined and is of great clinical importance. Patients were selected according to strict eligibility criteria rather than on the subjective basis of whether they were evaluated using CT or lumbar puncture. In addition to accuracy, other important measures were evaluated, including interobserver agreement, clinical acceptability, and potential effect on clinical practice.

Limitations

We acknowledge some potential limitations to this study. The inclusion criteria allowed for patients with non-thunderclap headaches to be enrolled by specifying a time of up to 1 hour from headache onset to peak intensity. Although this may have diluted the acuity, we note that the reported time to peak headache intensity was 1 hour in 6 patients with subarachnoid hemorrhage. This assessment criterion depended on patients' ability to accurately recollect the time interval from headache onset to peak intensity, and thus may be imprecise. In addition, we excluded patients with a history of 3 or more similar headaches (same intensity and character) in the past, over a time frame of greater than 6 months. This was intended to eliminate patients with chronic recurrent headaches, and these decision rules should not be applied to such patients. We recognize that physicians may overlook exclusion criteria when applying any decision rule and emphasize that such extrapolation is not evidence based. Headaches different from the patient's usual headache pattern likely need investigation and could represent a different etiology.[21]

Another potential limitation of this study was the lack of an established gold standard definition for subarachnoid hemorrhage. Given that some patients with small nonaneurysmal subarachnoid hemorrhage may be sent home, it may be worth restricting the diagnosis to patients with subarachnoid hemorrhage who require interventions. However, at present, we believe that our composite outcome is the optimal definition available.[22] Physicians also may not apply the rule correctly. Although this was the case for approximately 4% to 6% of the patients in this study, including very few with subarachnoid hemorrhage, it is possible that incorrect application of the decision rule may be more frequent with the addition of more variables in the Ottawa SAH Rule.

The Ottawa SAH Rule is also only for identifying patients with SAH; it is not an acute headache rule. As such, clinicians considering other diagnoses need to evaluate these as they would prior to the development of this rule. In particular, a patient who has a headache associated with an isolated cranial nerve palsy needs to be evaluated with angiography for an aneurysm that has increased in size and may be at risk for imminent rupture.[21,23]

Clinical and Research Implications

The Ottawa SAH Rule is a clinical decision rule that may help to standardize the investigation of acute headache among patients suspected of having subarachnoid hemorrhage without significantly changing current investigation rates. Patients at ultra-high risk (ie, those with >50% clinical pretest probability for subarachnoid hemorrhage) still warrant testing with CT, lumbar puncture, or both, given that they would have a posttest probability of greater than 1% for subarachnoid hemorrhage. This may include patients with strong family history or strong risk factors such as adult-onset polycystic kidney disease, although it is highly likely that these patients will have 1 or more of the high-risk features of the Ottawa SAH Rule.

The ultimate assessment of any clinical decision rule is assessing the benefits of implementation of the rule. Hence, an implementation study is the next step required to determine how the Ottawa SAH Rule performs in clinical practice, assess the actual effects on patient care and patient outcomes, and conduct a formal health economic analysis. Additional study could assess the relative benefits in rural vs urban settings.

Conclusions

Among patients presenting to the emergency department with acute nontraumatic headache that reached maximal intensity within 1 hour and who had normal neurologic examination findings, the Ottawa SAH Rule was highly sensitive for identifying subarachnoid hemorrhage. These findings only apply to patients with these specific clinical characteristics and require additional evaluation in implementation studies before the rule is applied in routine emergency clinical care.

ARTICLE INFORMATION

Author Affiliations: Department of Emergency Medicine, University of Ottawa, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada (Perry, Stiell, Symington); Department of Epidemiology and Community Medicine, University of Ottawa, Clinical Epidemiology Program, Ottawa Hospital Research Institute (Wells); Division of Neurosurgery, University of Ottawa, Clinical Epidemiology Program, Ottawa Hospital Research Institute (Lesiuk); University of Ottawa, Clinical Epidemiology Program, Ottawa Hospital Research Institute (Sutherland); Department of Emergency Medicine, Queen's University, Kingston, Ontario, Canada (Sivilotti); Department of Biomedical and Molecular Sciences, Queen's University (Sivilotti); Department of Emergency Medicine, University of

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016

British Columbia, Vancouver, British Columbia, Canada (Hohl); Department of Emergency Medicine, Université Laval, Quebec City, Quebec, Canada (Émond); Division of Emergency Medicine, McMaster University, Hamilton, Ontario, Canada (Worster); Division of Emergency Medicine, University of Toronto, Toronto, Ontario, Canada (Lee); Department of Emergency Medicine, University of Alberta, Edmonton, Alberta, Canada (Bullard, Mackey); Department of Emergency Medicine, University of Manitoba, Manitoba, Canada (Pauls).

Author Contributions: Dr Perry had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Perry, Sivilotti, Hohl, Émond, Lee, Lesiuk.
Acquisition of data: Perry, Sivilotti, Bullard, Hohl, Sutherland, Émond, Worster, Lee, Mackey, Pauls, Lesiuk, Symington.
Analysis and interpretation of data: Perry, Stiell, Sivilotti, Worster, Lee, Wells.
Drafting of the manuscript: Perry, Sutherland, Lee.
Critical revision of the manuscript for important intellectual content: Stiell, Sivilotti, Bullard, Hohl, Émond, Worster, Lee, Mackey, Pauls, Lesiuk, Symington, Wells.
Statistical analysis: Wells.
Obtained funding: Perry, Sivilotti, Émond, Lee.
Administrative, technical, or material support: Stiell, Sivilotti, Hohl, Sutherland, Lee, Pauls, Lesiuk, Symington.
Study supervision: Perry, Sivilotti, Bullard, Hohl, Sutherland, Worster, Mackey, Pauls.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This study was supported by peer-reviewed funding from the Canadian Institutes for Health Research (grant 153742). Dr Perry is supported by a Canadian Institutes for Health Research New Investigator Award and was previously supported as a Career Scientist by the Ontario Ministry of Health. Dr Stiell is a Distinguished Professor and University Health Research Chair, University of Ottawa. Dr Hohl was supported by a Mentored Clinician Scientist Award from the Vancouver Coastal Health Research Institute during the study period.

Role of the Sponsors: The funding organizations had no role in the design and conduct of the study; the collection, analysis, and interpretation of the data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Additional Contributions: We thank the hundreds of physicians who completed our data collection forms and the emergency department nurses and clerks at all of the study sites for their cooperation. We thank Albert E. Lauwers, MD, FRCP (Office of the Coroner of Ontario), for assistance in verifying outcomes; Dr Lauwers received no compensation for his contributions. We also thank the following research personnel at the study hospitals: *Vancouver General Hospital, Vancouver, British Columbia:* Jan Buchanan; *Ottawa Hospital—Civic Campus and General Campuses, Ottawa, Ontario:* Juanita Wilzer, Renée Labreche; *University of Alberta, Edmonton, Alberta:* Harris Lari, Leslie Saunders, Ginny Willis, Sandy Sandilands; *Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario:* Deborah Wright, Johanna Pak; *Kingston General Hospital, Kingston, Ontario:* Kathy Bowes, Jane Reid, Deborah Emerton; *Hôpital de L'Enfant-Jésus, Quebec City, Quebec:* Patricia Chabot; *Hamilton Health Sciences Centre, Hamilton, Ontario:* Christina Brean; *Lethbridge Regional Hospital, Lethbridge, Alberta:* Marlene Myles; *Winnipeg Health Sciences Centre, Winnipeg, Manitoba:* Irene Osinchuk. We thank our Ottawa Hospital Research Institute colleagues Sarai Cohn-Kalter, Malaika Mvungi, Sheryl Domingo, My-Linh Tran, Catherine Clement, and Angela Marcantonio for their assistance with this project.

Previous Presentation: Presented in part at the CAEP 2012 conference of the Canadian Association of Emergency Physicians, Niagara Falls, Ontario, Canada, June 2-6, 2012.

REFERENCES

1. Edlow JA, Panagos PD, Godwin SA, Thomas TL, Decker WW; American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. *Ann Emerg Med*. 2008;52(4):407-436.

2. Vermeulen M, van Gijn J. The diagnosis of subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry*. 1990;53(5):365-372.

3. Perry JJ, Stiell IG, Wells GA, Spacek AM. Diagnostic test utilization in the emergency department for alert headache patients with possible subarachnoid hemorrhage. *CJEM*. 2002;4(5):333-337.

4. Morgenstern LB, Huber JC, Luna-Gonzales H, et al. Headache in the emergency department. *Headache*. 2001;41(6):537-541.

5. Weir B. Headaches from aneurysms. *Cephalalgia*. 1994;14(2):79-87.

6. Vermeulen MJ, Schull MJ. Missed diagnosis of subarachnoid hemorrhage in the emergency department. *Stroke*. 2007;38(4):1216-1221.

7. Perry JJ, Stiell IG, Sivilotti ML, et al. Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of subarachnoid haemorrhage: prospective cohort study. *BMJ*. 2011;343:d4277.

8. Evans RW, Armon C, Frohman EM, Goodin DS. Assessment: prevention of post-lumbar puncture headaches: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2000;55(7):909-914.

9. Wasson JH, Sox HC, Neff RK, Goldman L. Clinical prediction rules: applications and methodological standards. *N Engl J Med*. 1985;313(13):793-799.

10. Laupacis A, Sekar N, Stiell IG. Clinical prediction rules: a review and suggested modifications of methodological standards. *JAMA*. 1997;277(6):488-494.

11. McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS; Evidence-Based Medicine Working Group. Users' Guides to the Medical Literature: XXII: how to use articles about clinical decision rules. *JAMA*. 2000;284(1):79-84.

12. Stiell IG, Wells GA. Methodologic standards for the development of clinical decision rules in emergency medicine. *Ann Emerg Med*. 1999;33(4):437-447.

13. Perry JJ, Stiell IG, Sivilotti ML, et al. High-risk clinical characteristics for subarachnoid haemorrhage in patients with acute headache: prospective cohort study. *BMJ*. 2010;341:c5204.

14. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. *Lancet*. 1974;2(7872):81-84.

15. Tsementzis SA, Hitchcock ER, DeCothi A, Gill JS. Comparative studies of the diagnostic value of cerebrospinal fluid spectrophotometry and computed tomographic scanning in subarachnoid hemorrhage. *Neurosurgery*. 1985;17(6):908-912.

16. Sames TA, Storrow AB, Finkelstein JA, Magoon MR. Sensitivity of new-generation computed tomography in subarachnoid hemorrhage. *Acad Emerg Med*. 1996;3(1):16-20.

17. Perry JJ, Sivilotti MLA, Stiell IG, et al. Should spectrophotometry be used to identify xanthochromia in the cerebrospinal fluid of alert patients suspected of having subarachnoid hemorrhage? *Stroke*. 2006;37(10):2467-2472.

18. van der Wee N, Rinkel GJE, Hasan D, van Gijn J. Detection of subarachnoid haemorrhage on early CT: is lumbar puncture still needed after a negative scan? *J Neurol Neurosurg Psychiatry*. 1995;58(3):357-359.

19. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-174.

20. Perry JJ, Eagles D, Clement CM, et al. An international study of emergency physicians' practice for acute headache management and the need for a clinical decision rule. *CJEM*. 2009;11(6):516-522.

21. McBeath JG, Nanda A. Case reports: sudden worsening of cluster headache: a signal of aneurysmal thrombosis and enlargement. *Headache*. 2000;40(8):686-688.

22. Perry JJ, Symington C, Mansour M, Taljaard M, Stiell IG. Is this subarachnoid hemorrhage significant? a National Survey of Neurosurgeons. *Can J Neurol Sci*. 2012;39(5):638-643.

23. Kissel JT, Burde RM, Klingele TG, Zeiger HE. Pupil-sparing oculomotor palsies with internal carotid–posterior communicating artery aneurysms. *Ann Neurol*. 1983;13(2):149-154.

Downloaded From: http://jama.jamanetwork.com/ on 02/05/2016