How to Determine if this Headache is a Subarachnoid Hemorrhage

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CAEP 2015
Nothing to Declare
Objectives

- Identify which headache patients are at high risk for subarachnoid hemorrhage as determined by The Ottawa SAH Rule
- Highlight the evidence behind The Ottawa SAH Rule
- Determine if a CT head is sufficient to rule out subarachnoid hemorrhage
- Learn how to interpret CSF Results that are not quite normal
- Discuss when cerebral angiography is required
Who To Investigate - Case 1

- 38 year old male with history of migraine, presents with headache - started 4 hours previously, onset to peak in 10 minutes, brother brought ED by car
- Pain is 8/10, throbbing and diffuse, states headache different from previous (usually relieved with Advil)
- Physical exam: lying on stretcher, GCS 15, HR 80, BP 145/85, afebrile, supple neck, no focal deficits
What would you do?
Case 1 Continued

- CT done 5.75 hours after headache onset is normal
- LP done 7.5 hrs from onset, has no xanthochromia, RBCs $50 \times 10^6/L$ in final tube, $70 \times 10^6/L$ in first tube
- Now what?
Case 1 Continued

- Patient had complete pain relief following metoclopramide 10mg IV
- Patient discharged home
- Follow-up at 1 and 6 months found patient did not subsequently have a SAH
Summary Case 1

- Determining who is at risk for SAH can be difficult
- Is an early CT enough to rule out SAH?
- How significant are small numbers of RBCs in the CSF?
- More investigations do not always help!
Subarachnoid Hemorrhage: The Clinical Problem

- 2.5 to 4.5% of emergency department (ED) visits are for headache
- Only 1% of these headaches are subarachnoid hemorrhages (SAH)
- Many patients are over-investigated with expensive and invasive procedures
- 1 in 20 SAH patients are misdiagnosed at time of first ED visit; highest among low acuity patients in smaller centres
- Mortality of SAH is 50%; with 42% of SAH survivors having permanent neurological deficits
Development of a SAH Clinical Decision Rule

0. Use / Yield of Current Testing (N=891)
   *CJEM 2002*

I. Development of the Rules (N=1,999)
   *BMJ 2010*

IIa. Sensitivity of Early CT for SAH (N=3,123)
    *BMJ 2011*

IIb. Validation with Refinement (N=2,131)
    *JAMA 2013*

IIc. Distinguishing SAH from Traumatic Tap (N=1,739)
    *BMJ 2015*

III. Validation of Ottawa SAH Rule (N=1,140)
    *SAEM 2014*
Clinical Decision Rules to Rule Out Subarachnoid Hemorrhage for Acute Headache

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**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 features.
### Classification Performance Rule 1

132 SAH Cases (N=2,131)

<table>
<thead>
<tr>
<th>Rule</th>
<th>SAH</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>High Risk</td>
<td>130</td>
<td>1,447</td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>2</td>
<td>552</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>Investigate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>98.5%</td>
<td>27.6%</td>
<td>99.6%</td>
<td>74.0%</td>
</tr>
</tbody>
</table>

(94.6-99.6) (25.7-29.6) (98-100)
Refined Rule – The Ottawa SAH Rule

Variables in Rule 1

- Symptom of neck pain
- Onset with exertion
- Age ≥ 40 years
- Witnessed loss of consciousness

Plus

- Thunderclap headache (instantly peaking)
- Neck stiffness on examination (with flex)
## Classification Performance of The Ottawa SAH Rule

### 132 SAH Cases (N=2,131)

<table>
<thead>
<tr>
<th>Rule</th>
<th>SAH</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>High Risk</td>
<td>132</td>
<td>1,694</td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>0</td>
<td>305</td>
<td></td>
</tr>
</tbody>
</table>

- **Sensitivity**: 100% (97.2-100)
- **Specificity**: 15.3% (13.8-16.9)
- **NPV**: 100% (98-100)
- **Investigate**: 85.7%
Prospective Validation of The Ottawa SAH Rule

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Phase III: Prospective Validation of The Ottawa SAH Rule

Rationale

- Given Rule was altered, additional validation is needed

Objectives

- To validate the Ottawa SAH Rule in a new cohort of ED patients with acute headache
- Determine the performance of the rule for SAH
Inclusion Criteria

- Alert patients >15 years with a non-traumatic acute headache
- “Alert” is a GCS=15
- “Non-Traumatic” is no direct head trauma in previous 7 days
- “Acute” is maximal pain in **<1 hour** and presents **within 14 days**
Exclusion Criteria

- Confirmed SAH
- 3 or more similar (character and intensity) headaches in past
- Already investigated with both CT and LP
- New neurological deficits
- Previous aneurysm or SAH
- CNS neoplasm
Eligible Patients
N=1,558

Patients Enrolled
N=1,140 (73.2%)

SAH
N=64

Missed Eligible Patients
N=418

Patients Lost to Follow-up
N=4
### Phase III: Prospective Validation of The Ottawa SAH Rule

**64 SAH Cases (N=1,140)**

<table>
<thead>
<tr>
<th>Rule</th>
<th>SAH</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>High Risk</td>
<td>64</td>
<td>922</td>
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<tr>
<td>Low Risk</td>
<td>0</td>
<td>154</td>
</tr>
</tbody>
</table>

**Sensitivity** 100% (94.3-100)

**Specificity** 14.3% (11.7-15.6)

**Investigate** 86.5%

**Baseline CT Rate** 87.1%
**Combined Validation of The Ottawa SAH Rule**

**196 SAH Cases (N=3,271)**

<table>
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<tr>
<th>Rule</th>
<th>SAH</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>High Risk</td>
<td>196</td>
<td>2616</td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>0</td>
<td>459</td>
<td></td>
</tr>
</tbody>
</table>

**Sensitivity:**
- Yes: 100%
- No: (97.9-100)

**Specificity:**
- Yes: 16.7%
- No: (15.3-18.2)
The Ottawa SAH Rule –
Clinical Implications

- The Ottawa SAH Rule is ready to use!
- High risk patients should be investigated for SAH
- Low risk patients, or those not meeting eligibility criteria should be managed symptomatically or assessed for other conditions
Ottawa SAH Rule

For alert patients > 15 years with new severe non-traumatic headache reaching maximum intensity within 1 hour

Not for patients with new neurological deficits, previous aneurysms, SAH, brain tumors, or history of similar headaches (≥ 3 episodes over ≥ 6 months)

Requires Investigation if one or more findings present:

- Symptom of neck pain or stiffness
- Age ≥ 40 years
- Witnessed loss of consciousness
- Onset during exertion
- Thunderclap headache (peak pain instantly)
- Limited neck flexion on exam

○ NO

Does not need investigation for SAH

○ YES

Requires investigation for SAH
When a Headache is a Subarachnoid Hemorrhage is a CT Enough to Rule it Out?

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Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of subarachnoid haemorrhage: prospective cohort study

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Results: Flow of Patients

Enrolled Patients
N=3,132 (240 SAH)

CT ≤ 6 hours from Headache Onset
N=953

CT ≤ 6 hours from Headache Onset
SAH=121

CT > 6 hours from Headache Onset
N=2,179

CT > 6 hours from Headache Onset
SAH=119
Classification Performance Overall for 240 SAH Cases (N=3,132)

<table>
<thead>
<tr>
<th>CT Positive</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>223</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
<td>2,892</td>
</tr>
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</table>

Sensitivity: 92.9% (89.0-95.5)
Specificity: 100% (99.9-100)
Classification Performance with CT>6 Hours from Headache Onset for 119 SAH Cases (N=2,179)

<table>
<thead>
<tr>
<th>CT Positive</th>
<th>SAH</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>102</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
<td>2,060</td>
</tr>
</tbody>
</table>

Sensitivity: 85.7% (78.3-90.9)  
Specificity: 100% (99.8-100)
Classification Performance with $CT \leq 6$ Hours from Headache Onset for 121 SAH Cases ($N=953$)

<table>
<thead>
<tr>
<th>CT Positive</th>
<th>SAH</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>121</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>0</td>
<td>832</td>
</tr>
</tbody>
</table>

- **Sensitivity**: 100% (97.0–100)
- **Specificity**: 100% (99.5–100)
Discussion

- 3 CTs misdiagnosed by EP as normal
- 1 CT initially misdiagnosed negative by radiologist
- Timing of 15 cases with negative CT with positive LP were from 8 hours to 8 days
- Of 15 missed SAH, only 5 required surgery
One Patient with Early CT was Recently Missed

- 52 yr female, with a sudden headache, her second within a week, had a scan at 4.5 hours after her most recent headache
- Normal scan
- Had a LP with 50,000 RBCs, + xant (after 3 failed attempts, obtained by anesthesia about 7.5 hours post headache)
- Had CTA, no aneurysm, but had a dural fistula (an artery connects with a dural vein/sinus)
- Underwent surgical repair
Another Patient with Early CT was Missed

- 27 yr female, with history of sickle cell anemia with a baseline hemoglobin of 60 had a sudden headache over right side of head with max pain at onset
- Max pain lasted 10 mins then lessened
- Normal scan 3 hours post onset
- Had a LP with thousands RBCs with one attempt
- Had CTA, with aneurysm 3mm posterior circulation
- Underwent coiling
Conclusions

- Largest prospective study determining the sensitivity of CT in alert acute headache ED patients
- Experienced neuro-radiologist should ideally interpret all scans, ideally in real-time
- When CT done > 6 hours, must be followed by LP
- When CT done ≤ 6 hours from headache onset, CT is sensitive enough to exclude SAH without an LP for most patients
LP: How Do We Interpret CSF Results?

- CSF results are often not completely normal due to a traumatic tap.
- We conducted a substudy of the combined derivation and validation datasets.
- Assessed LP results to determine if there are cut points which can safely exclude aneurysmal SAH.
Differentiation between traumatic tap and aneurysmal subarachnoid hemorrhage: prospective cohort study

Jeffrey J Perry,1 Bader Alyahya,1 Marco L A Sivilotti,2 Michael J Bullard,3 Marcel Émond,4 Jane Sutherland,5 Andrew Worster,6 Corinne Hohl,7 Jacques S Lee,8 Mary A Eisenhauer,9 Merrill Pauls,10 Howard Lesiuk,11 George A Wells,12 Ian G Stiell1

ABSTRACT
OBJECTIVES
To describe the findings in cerebrospinal fluid from patients with acute headache that could distinguish subarachnoid hemorrhage from the effects of a traumatic lumbar puncture.

DESIGN
A substudy of a prospective multicenter cohort study.

SETTING
12 Canadian academic emergency departments, from November 2000 to December 2009.

PARTICIPANTS
Alert patients aged over 15 with an acute non-traumatic headache who underwent lumbar puncture to rule out subarachnoid hemorrhage.

MAIN OUTCOME MEASURE
Aneurysmal subarachnoid hemorrhage requiring intervention or resulting in death.

RESULTS
Of the 1739 patients enrolled, 641 (36.9%) had abnormal results on cerebrospinal fluid analysis with $>1 \times 10^6$ red blood cells in the first tube of 100,000 person-years.12 When a patient presents to the emergency department with sudden severe headache, traditional teaching is to perform computed tomography of the brain and, if the results are negative for subarachnoid hemorrhage, carry out a lumbar puncture to analyze the cerebrospinal fluid to exclude that diagnosis.2-4 The sensitivity of modern thin sliced computed tomography for subarachnoid hemorrhage is 100% (95% confidence interval 97% to 100%) when it is performed within six hours of onset of the headache. If it is carried out after six hours, however, its sensitivity decreases to 85.7% (78.3% to 90.6%).7 Therefore, if the scan is performed more than six hours after headache onset and is negative for subarachnoid hemorrhage, the physician will typically perform lumbar puncture to rule it out.

Unfortunately, it can be difficult to differentiate whether the blood in the cerebrospinal fluid results from trauma related to the lumbar puncture itself or from a subarachnoid hemorrhage. A so-called "traumatic tap" is estimated to occur in 10–30% of lumbar punctures, rendering the procedure non-diagnostic and often resulting in additional testing and diagnostic
Study Flow

Total = 4,121

LP done = 1,739
(42.1%)

Abnormal LP = 641
(36.9%)

Normal LP = 1,098
(63.1%)

Aneurysmal SAH = 15
(2.3%)

No Aneurysmal SAH = 626
(97.7%)

(-) Xanthochromia = 8

(+) Xanthochromia = 7
## Classification Performance of Abnormal LP for Aneurysmal SAH (N=641)

<table>
<thead>
<tr>
<th>RBCs &lt;2,000 x 10^6/L and No Xant</th>
<th>SAH</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>15</td>
<td>55</td>
</tr>
<tr>
<td>High Risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>0</td>
<td>571</td>
<td></td>
</tr>
</tbody>
</table>

### Sensitivity
- **Sensitivity** = 100.0%
- (74.7%-100%)

### Specificity
- **Specificity** = 91.2%
- (88.6%-93.3%)
Summary of CSF Interpretation

- If no visual xanthochromia and RBCs in last tube <2,000 x 10⁶/L patient is low risk, so unless patient “ultra high risk” stop

- If patient has ≥2,000 x 10⁶/L in last tube proceed to angiography

- If xanthochromia present patient has a SAH
When to Order Cerebral Angiography (CTA)

- Clear evidence does not exist!
- 1% - 5% of the general population has a cerebral aneurysm
- Most aneurysms will never cause harm, treating them may result in stroke or other surgical harms

My Suggestion:

- If CSF is “high risk” or patient is “ultra high risk” without completely normal LP get CTA
- If there is a time lag > 1 week or there is a contraindication to LP get CTA
- If the CT is positive order CTA
- All other cases do not order due to incidental aneurysms
Summary

- Use The Ottawa SAH Rule to safely identify which patients with headache require investigations for SAH.
- Use of CT alone is appropriate for most patients, only “ultra high risk” patients need further assessment.
- LPs diagnose very few aneurysmal SAHs.
- No xanthochromia and a RBC count of <2,000 x 10^6/L in the final tube is a “low risk LP”.
- Patients with a “high risk LP”, or are “ultra high risk” by history without a completely normal LP, or present late should undergo cerebral angiography.