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ORIGINAL RESEARCH

Sensitivity of proposed clinical decision rules for subarachnoid haemorrhage: An external validation study

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Abstract

***Objectives*:** Subarachnoid haemorrhage (SAH) is an uncommon but important cause of sudden-onset headache. Three clinical decision rules (CDRs) for investigation in sudden headache have been proposed, but concerns were raised about the generalisability of some variables. Our aim was to determine what proportion of patients with confirmed SAH has the identified high-risk factors and the sensitivity of the proposed CDR in an Australasian cohort.

***Methods*:** This is a retrospective cohort study of alert and neurologically intact adult patients with confirmed SAH attending two community teaching hospitals between 2000 and 2011. The outcomes of interest were the proportion of patients with each high-risk criterion (descriptive statistics) and sensitivity of each proposed CDR (%, interquartile range [IQR]).

***Results*:** There were 59 confirmed SAH that met the inclusion criteria. Sensitivity of proposed CDR 1 was 96.6% (95% confidence interval [CI] 88.5–99.1%), sensitivity of proposed CDR 2 was 100% (95% CI 93.9–100%) and sensitivity of proposed CDR 3 was 89.8% (95% CI 79.5–95.3%). The addition of vomiting to the criteria in CDRs 1 and 3 increased the sensitivity of both these CDRs to 100%.

***Conclusion*:** CDR 2, or the refinement of CDRs 1 and 3 with the inclusion of at least one episode of vomiting as a criterion, has very high sensitivity. Although unlikely to reduce CT scan rates for patients in whom there is a clinical suspicion of SAH, they might be useful in guiding which patients require further testing (e.g. lumbar puncture) after a negative CT scan.

Key words: *clinical decision rule, headache, subarachnoid.*

Key findings

- Proposed clinical decision rule 2 had 100% sensitivity for subarachnoid haemorrhage.
- With the addition of vomiting to the criteria, proposed clinical decision rules 1 and 3 achieved 100% sensitivity for subarachnoid haemorrhage.
- In this study, all cases of subarachnoid haemorrhage were diagnosed on CT scan.

Introduction

Subarachnoid haemorrhage (SAH) is an uncommon but potentially life-threatening cause of headache presenting to EDs.[1–4] For patients with altered conscious state or neurological deficit, the decision to investigate is easy. Alert, neurologically intact patients pose the challenge. Investigation is time consuming and not without risk; however, a missed diagnosis of SAH can have catastrophic consequences.[4] Investigation for suspected SAH includes non-contrast head CT and, if that is negative, a lumbar puncture (LP) is recommended. The vast majority of CT scans (>95%) are normal,[2] and it can be hard to distinguish a traumatic tap from true SAH on LP.[5] Ideally, we would only investigate higher-risk patients where the risks and inconvenience of investigation were outweighed by the risks of the potential illness.

Perry *et al.*,[6] in a large prospective trial, have identified factors that are associated with high risk of SAH and have proposed that these might form the basis of an accurate clinical decision rule (CDR) regarding the need for investigation for SAH in patients with acute headache. The factors identified were age >40 years, complaint of neck pain or stiffness, witnessed loss of consciousness, onset with exertion, arrival by ambulance, vomiting at least once, diastolic BP >100 mmHg and systolic BP >160 mmHg. Three draft CDRs were developed for further testing. These are shown in Table 1. For each rule, a patient would be investigated if one or more of the criteria are present. In derivation, each

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TABLE 1. *Proposed clinical decision rules for subarachnoid haemorrhage*

Rule number	Variable	Sensitivity (*n*, %, 95% CI)
1	Age >40 years Complaint of neck pain or stiffness Witnessed loss of consciousness Onset with exertion	57/59, 96.6% 88.5–99.1%
2	Arrival by ambulance Age >45 years Vomited at least once Diastolic BP >100 mmHg	59/59, 100% 93.9–100%
3	Arrival by ambulance Systolic BP >160 mmHg Complaint of neck pain or stiffness Age 45–55 years	53/59, 89.8% 79.5–95.3%

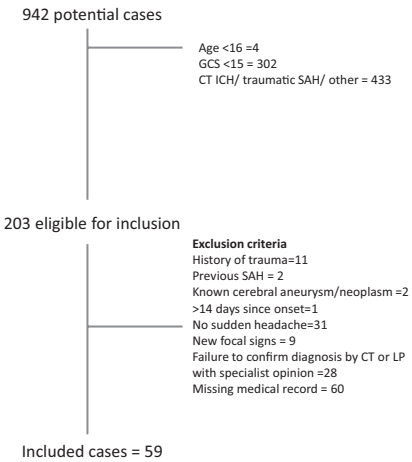

Figure 1. *Sample derivation. ICH, intracranial haemorrhage; LP, lumbar puncture; SAH, subarachnoid haemorrhage.*

rule was 100% sensitive and about 30% specific. The authors raised concerns about the generalisability of the factors, especially arrival by ambulance, which might differ between prehospital care systems. In their sample, >50% of patients with SAH arrived by ambulance. To date, there is no data to compare this with an Australian population. The objective of the present study was to determine what proportion of patients with confirmed SAH has the above factors and to determine the sensitivity of the proposed CDR in an Australasian cohort.

Methods

This was a retrospective cohort study performed by medical record review. Cases were adult patients aged greater than 16 years with confirmed SAH presenting to the ED of two community teaching hospitals without specialist neurosurgical units in Melbourne, Australia, between 2000 and 2011. The combined annual ED census is approximately 110 000.

Potential cases were identified from the ED data management database by final ED diagnosis of 'subarachnoid haemorrhage, non-traumatic' or 'haemorrhage, intracranial, non-traumatic'. Patients were excluded if they were aged <16 years, had a history of trauma within the last 7 days (collapse associated with onset of headache leading to head injury was not an exclusion), history of previous SAH, known cerebral aneurysm or cerebral neoplasm, it was more than 14 days from symptom onset, there was absence of 'sudden' headache, there was a history of three or more headaches with similar characteristics and intensity over more than 6 months, GCS was <15, there were new focal neurological signs or there was failure to confirm the diagnosis of SAH by CT head scan, CT angiography, conventional angiography, MRI or LP supported by specialist neurosurgical opinion. These are consistent with the derivation study.[6] Where a patient was transferred to the regional neurosurgical centre without a confirmed diagnosis, data were collected at that site regarding further investigations and final diagnosis.

Data were collected from the medical record and electronic radiology reporting systems onto piloted data collection forms, and included assessment against each of eight criteria in Table 1. Criteria not reported were assumed to be absent. Data collectors were not blinded to study hypotheses. Interrater reliability for data collection was tested for 10% of cases for the data items age, sex, ED diagnosis of SAH, CT scan performed, sudden onset headache, vomiting, witnessed loss of consciousness and arrival by ambulance. Agreement was 100% for all items.

The outcomes of interest were the proportion of patients with each criterion (descriptive statistics) and sensitivity of each proposed CDR (with 95% confidence intervals [CIs]). The sample size was governed by the number of confirmed cases. Preliminary data suggested about 500 patients with an ED diagnosis of SAH, of whom we expected ~20% to be GCS 15. This would give us a final sample of about 100, which would be sufficient to provide a CI <5%.

Ethics approvals were obtained from the relevant institutional ethics committees (Western Health Low Risk Ethics Panel and Royal Melbourne Hospital HREC) and patient consent for participation was not required.

Results

Sample derivation is shown in Figure 1. There were 59 confirmed SAH that met the inclusion criteria. All cases were diagnosed on CT (100%, 95% CI 93.9–100%). Prevalence of the criteria used in the CDR is shown in Table 2.

Sensitivity of proposed CDR 1 was 96.6% (95% CI 88.5–99.1%; two cases missed), sensitivity of proposed CDR 2 was 100% (95% CI 93.9–100%) and sensitivity of proposed CDR 3 was 89.8% (95% CI 79.5–95.3%; six cases missed). The addition of vomiting to the criteria in CDRs 1 and 3 increased the sensitivity of both these CDRs to 100%. Characteristics of missed patients are shown in Table 3.

Discussion

SAH is an uncommon but important cause of headache of sudden onset.

TABLE 2. *Prevalence of variables comprising the proposed CDRs*

Variable		
Age (*n*, %)	>40 years	47, 80
	>45 years	41, 69
	45–55 years	16, 27
Complaint of neck pain or stiffness (*n*, %)		25, 42
Onset with exertion (*n*, %)		12, 20
Witnessed loss of consciousness (*n*, %)		11, 19
Arrival by ambulance (*n*, %)		41, 70
Vomited at least once (*n*, %)		39, 66
Diastolic blood pressure >100 mmHg (*n*, %)		6, 10
Systolic BP >160 mmHg (*n*, %)		18, 31

CDR, clinical decision rule.

Investigation to rule it out is time consuming and not without risk. Ideally, we would only investigate higher-risk patients where the risks and inconvenience of investigation were outweighed by the potential risks of the condition. The appetite of clinicians for an accurate risk stratification tool or CDR to guide investigation in patients with sudden headache has been demonstrated in an international survey.[7] CDRs are tools that help clinicians make diagnostic and therapeutic decisions at the bedside. They are derived from original research and incorporate three or more variables from history, examination or simple tests. In a derivation study, Perry *et al.* derived three proposed CDRs.[6] The authors expressed concern that some of the variables (in particular, arrival by ambulance) might not be generalisable to other health systems – a question the present study has tried to answer.

Our results show that CDR 2 (any of arrival by ambulance, age >45, vomited at least once and diastolic BP >100mHg) was 100% sensitive and that the other CDRs would have missed up to 10% of patients. Refining either of these with the additional criterion of vomited at least once resulted in 100% sensitivity.

Like Perry *et al*.,[6] our study had a high proportion of patients with SAH arriving at hospital by ambulance. CDRs 2 and 3 include this as a criterion. The Canadian and Australian health systems are quite similar. In health systems with a different pattern of ambulance use, these CDRs might not perform as well. For these settings, the refined version of CDR 1 (including vomiting) might be more accurate. Further data are needed to clarify this.

Since we began our study, two studies validating one or more of Perry *et al*.'s CDR have been undertaken. Perry *et al*.[8] have reported a multisite validation of the CDR reporting sensitivities of between 95.5 and 98.5% (Table 4). Based on that data, they derived a refined CDR (the Ottawa SAH CDR) that recommends investigation if any of the following features are present: age >40, neck pain or stiffness, witnessed loss of consciousness, onset during exertion, thunderclap headache (instantly peaking pain) or limited neck flexion on examination. This has 100% sensitivity, but specificity was about half that of the previously derived CDR (Table 4). In addition, we have some concerns that the new criteria (thunderclap headache and limited neck flexion) might be more prone to subjective interpretation. Unfortunately, as our data collection was limited to the criteria identified in the Perry *et al*.'s derivation study[6] and did not include instantly peaking headache and limited neck flexion, we were unable to test the refined CDR.

Mark *et al*.[9] took a different approach investigating the sensitivity of CDR 1 in a case-control study of CT negative patients investigated for SAH. The rationale for this study was that cranial CT in acute headache is not only aimed at identifying SAH. Other serious diagnoses such as intracranial haemorrhage and brain tumours often require exclusion. They argue that the more relevant clinical question is which CT negative patients with symptoms suggestive of SAH require further investigation with LP, angiography or CT angiography. They reported a sensitivity of 97.1% for CDR 1 with a negative likelihood ratio (LR) of 0.13.

The accumulated data suggest that existing or refined CDRs have high sensitivity. Although the original intention of the CDR was to identify a group of patients with headache for whom investigation (CT and LP) might be avoided,[6] in our opinion, the most likely application of these CDRs would be in a stepwise Bayesian decision-making process. The rationale for our opinion is that SAH is not the only pathology being excluded and the 95% CI of the CDR are outside most clinicians' risk tolerance. If it is assumed that the incidence of SAH in neurologically normal patients presenting to ED with sudden headache is approx. 7%,[6,10] and that a negative non-contrast cranial CT scan has a negative LR of 0.07 (assumes sensitivity 93% and specificity 99.9%), the post-test probability of SAH would be 0.49%, or approximately 1 in 200 patients. Application of CDR 1, shown to have a negative LR of 0.13 in CT negative patients,[9] would further reduce the post-test probability to 0.064%, about 1 in 1500 patients. This level is likely to be an acceptable level for clinicians, balancing the risks of missed diagnosis with those of additional testing. Given the specificity reported by Mark *et al*. of 22.7%, approximately one-quarter of LPs might be avoided. That said, it should also be remembered that an important step in Bayesian decision-making is risk stratification for SAH before the results of the CT to avoid a negative CT result unduly influencing decision-making regarding the need for a LP.

The present study has some limitations that should be considered when interpreting the results. Patients were identified from an ED database. Although a wide identification strategy was used with the aim of identifying all non-traumatic intracranial haemorrhages of which SAH is a subset, it is possible that some miscoding has led to unidentified cases. It is also possible that some SAHs were missed if

TABLE 3. *Characteristics of missed patients*

Characteristics	Patient no. 1	2	3	4	5	6
Age (years)	32	21	28	31	62	34
Sex	Male	Male	Female	Male	Female	Male
Missed by CDR number(s)	1,3	1,3	3	3	3	3
Age >40 years	No	No	No	No	Yes	No
Age >45 years	No	No	No	No	Yes	No
Age 45–55 years	No	No	No	No	No	No
Neck pain or stiffness	No	No	No	No	No	No
Witnessed loss of consciousness	No	No	No	Yes	No	No
Onset with exertion	No	No	Yes	No	No	No
Arrival by ambulance	No	No	No	No	No	No
Vomited at least once	Yes	Yes	Yes	Yes	Yes	Yes
Diastolic BP >100 mmHg	No	No	No	No	No	No
Systolic BP >160 mmHg	No	No	No	No	No	No

CDR, clinical decision rule.

TABLE 4. *Performance of CDR and refinements in validation studies*

	CDR 1	CDR 2	CDR 3	Ottawa CDR
Sensitivity				
Perry *et al.*[6]	100%	100%	100%	*
Perry *et al.*[8]	98.5%	95.5%	97%	100%
Mark *et al.*[9]	97.1%	*	*	*
Present study	96.6%	100%	89.8%	*
Pooled sensitivity (Perry *et al.*,[6,8] present study)†	98.8%	98.1%	96.9%	
Specificity				
Perry *et al.*[6]	28.4%	36.5%	38.8%	
Perry *et al.*[8]	27.6%	30.6%	35.6%	15.3%
Mark *et al.*[9]	22.7%	*	*	*
Negative predictive value				
Perry *et al.*[6]	100%	100%	100%	*
Perry *et al.*[8]	99.6%	99%	99.4%	100%
Negative likelihood ratio				
Perry *et al.*[8]	0.054	0.127	0.099	0.024
Mark *et al.*[9]	0.13	*	*	*
Investigation rate				
Perry *et al.*[6]	73.5%	65.8%	63.7%	*
Perry *et al.*[8]	74%	71%	63.7%	85.7%

*Not reported. †Pooled by aggregation. CDR, clinical decision rule.

patients with a negative CT did not have a LP or if the possibility of SAH was not considered and investigated for by treating clinicians. Data collection was based on medical record review. Although age, ambulance arrival and BP parameters are reliably recorded, it is possible that the features on history (neck pain or stiffness, vomiting, witnessed loss of consciousness and onset with exertion) might be subject to reporting error. That said, such omissions would tend to underestimate the sensitivity of the CDR. The methodology used did not allow calculation of specificity or negative predictive value. We considered using a case-control methodology, but felt that, without any way to determine from medical records the physician's pretest probability for the differential diagnoses under consideration, accurate case control matching was not possible, and that results obtained from such an analysis would be questionable. Thus, we limited our study to a simple descriptive cohort. The present study was also unable to determine the proportion of CT or LPs that might be avoided. If this is low, the clinical utility of the CDR would be challenged. Despite using a wide enrolment window, we fell short of our

target of 100 patients. This is largely because older inactive records has been converted to microfilm and were not possible to access. The present study was conducted in a single health system and might not be generalisable to other systems.

Conclusion

CDR 2, or the refinement of CDRs 1 and 3 with the inclusion of at least one episode of vomiting as a criterion, has very high sensitivity. Although unlikely to reduce CT scan rates for patients in whom there is a clinical suspicion of SAH, they might be useful in guiding which patients require further testing (e.g. LP) after a negative CT scan. Further research to evaluate such an approach is warranted.

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Author contributions

A-MK had the concept of the present study; SE, NM, SK and A-MK designed the study and collected data; A-MK performed the analysis and wrote the first draft of the present paper; all authors contributed to the refinement of the manuscript.

Competing interests

A-MK is a member of the editorial board for *Emergency Medicine Australasia*.

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