

To LP or not to LP? A service evaluation investigating the prevalence of subarachnoid haemorrhage in patients undergoing a lumbar puncture in the acute medical setting

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Abstract

Subarachnoid haemorrhage (SAH) is a potentially life-threatening cause of acute severe headache. This service evaluation aimed to investigate the prevalence of SAH in patients referred to acute medicine with acute severe headache who underwent a lumbar puncture (LP) at a tertiary teaching hospital, over a four-year period. Of the 677 samples analysed for CSF bilirubin, 619 were negative (91.5%), 48 indeterminate (7%), and 10 classified as positive (1.5%). Only one patient (0.1%) was diagnosed with an aneurysmal SAH and underwent intervention. Therefore, the diagnostic yield of an LP to exclude SAH in this setting is extremely low. This service evaluation challenges the dogma that LP is necessary in all patients with acute severe headache.

Keywords

Subarachnoid haemorrhage, intracranial aneurysm, Cerebrospinal Fluid, lumbar puncture, internal medicine

Key points

1. Subarachnoid haemorrhage is rare in patients presenting with headache to the acute medical take.
2. The diagnostic yield of an LP to exclude subarachnoid haemorrhage is low.
3. If an LP is indicated, should it be performed semi-electively during normal working hours?

Introduction

Headache accounts for 1-2% of emergency department (ED) attendances¹⁻³. In the ED and acute medical setting, the main diagnostic challenge is differentiating between benign and life-threatening causes of headache⁴. Subarachnoid haemorrhage (SAH) is a potentially life-threatening cause of acute severe headache, resulting from the accumulation of blood between the arachnoid and pia mater. SAH is a relatively infrequent diagnosis with an incidence of 9 per 100,000 person-years, but it is associated with high mortality and morbidity; therefore, prompt diagnosis and appropriate management are paramount^{5,6}. The presentation can be non-specific, and differentiating SAH from other causes of acute severe headache can be difficult^{7,8}. A recent study of 976 patients presenting to an ED with a primary complaint of 'headache' over 6 months resulted in 52 patients undergoing a lumbar puncture (LP), none of which resulted in a diagnosis of SAH².

Following haemorrhage into the cerebrospinal fluid (CSF), oxyhaemoglobin liberated from red blood cells is converted to bilirubin. A high bilirubin

concentration causes a yellow discolouration of the CSF, commonly referred to as xanthochromia. The rule-out of SAH includes performing a computed tomography (CT) head scan, and if there is no neuroimaging evidence of SAH, an LP to exclude the presence of bilirubin in the CSF⁹. The National Institute for Health Excellence (NICE) guidance has recently been updated to state that if a CT head scan is performed within 6 hours of symptom onset and there is no evidence of SAH, an LP does not need to be routinely offered¹⁰. A CT head scan performed within 6 hours of symptom onset has been shown to have a negative predictive value for the detection of subarachnoid blood of 99.9%⁹.

Despite this, in acute medicine, it is still common practice to perform an LP to exclude the presence of increased CSF bilirubin in those with acute severe headache and no evidence of SAH on a CT head scan. The purpose of performing CSF bilirubin analysis is to identify small aneurysmal bleeds in which there is the potential to intervene before a potentially catastrophic haemorrhage. Performing an LP has associated risks

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(e.g. infection, post-LP headache and subdural/epidural haematoma). In addition, patients often require admission overnight on acute medical wards or remain in EDs whilst they await the procedure. Further data is needed surrounding the diagnostic utility of an LP to exclude SAH in those presenting to acute medicine with headache and a negative CT head scan. Furthermore, data are required to establish the safety of performing an LP in a semi-elective setting to facilitate earlier discharge in this group and support the move to ambulatory models of acute medical care.

This service evaluation aimed to investigate the prevalence of SAH in patients referred to acute medicine with headache who underwent an LP at a tertiary teaching hospital, over a four-year period.

Methods

Study design

This service evaluation retrospectively investigated all adult patients who underwent CSF bilirubin spectrophotometry analysis at the University Hospital of Wales (UHW) during a 4-year period between 1st April 2017 and 31st March 2021.

All patients aged 16 years or over who were reviewed or admitted by the acute medicine service at UHW in this timeframe were included. CSF samples sent from LPs performed outside of the ED/medical assessment unit, including the intensive care unit and neurology outpatients, were excluded. CSF samples with unknown locations were also excluded.

Biochemistry records were used to identify all requests for CSF bilirubin spectrophotometry between the 1st of April 2017 and the 31st of March 2021 at the UHW. Demographic data was obtained from electronic health records. CSF samples were analysed spectrophotometrically for bilirubin and oxyhaemoglobin using the Uvicon xs, Northstar Scientific UV-visible spectrophotometer. In-house positive quality control samples were routinely run with every patient or run of samples. The results were interpreted according to the 2008 Revised National Guidelines¹¹. The results were categorised as positive, indeterminate, or negative. Samples were classed as indeterminate if they were not protected from light, demonstrated an analytical interference or were not typically positive, but SAH could not be excluded as per the CSF interpretive guidelines.

Additionally, clinical coding records were used to identify all patients diagnosed with non-traumatic SAH between April 2017 and April 2022 based on ICD10 codes I60.0-I60.9. These data were matched with biochemistry records, therefore allowing for at least 1-year follow-up following LP. Electronic patient records were reviewed to determine the time of CT head scan, further relevant investigations, diagnosis

at discharge and clinical outcomes for patients with positive and indeterminate results. Individual case review was not conducted for the patients with negative CSF results, as none went on to have a SAH. Timing from CT head scan to LP was used instead of time of arrival to LP to account for a small number of patients who were discharged home to return the following day for LP.

The primary outcome was to determine the proportion of patients with SAH in our cohort. The secondary outcome was to determine the journey of patients undergoing an LP to investigate a possible SAH. The term ‘suspected SAH’ was used in electronic records when patients had negative imaging but positive/indeterminate CSF bilirubin results and a clinical history/examination in keeping with SAH.

Ethics

This service evaluation was undertaken with the retrospective analysis of routinely collected clinical data. As such, formal Research Ethics Committee review was not required, as confirmed by the NHS Health Research Authority. This service evaluation had the approval of the Cardiff and Vale University Health Board Information Department and Information Governance Team (QP785). We had consent from the patient to discuss their case.

Results

Between April 2017- March 2021, 902 samples were sent for CSF bilirubin spectrophotometric analysis, of which 677 were from patients undergoing an LP in the acute medical and ED settings at UHW. There was a significant difference in the sex of patients undergoing an LP (412 female (60.9%) and 265 male (39.1%) (p<0.0001)). The mean age was 41.1 years, and the range was 16-84 years (Table 1).

Table 1. Demographic data.

Baseline Demographics (n=677)	
Male n, %	265, 39.1%
Female n, %	412, 60.9%
Median age of all patients (IQR)	39 (23)
Waiting Times (hours)	
Median time to CT head from ED arrival (IQR)	3.03(3.06)
Median time to LP from CT head (IQR)	14.03 (15.22)
Timing of CT head scan (n, %)	
9am-9pm	432, 64.7%
9pm-9am	236, 35.3%
Timing of LP (n, %)	
9am-9pm	576, 85.2%
9pm-9am	100, 14.8%

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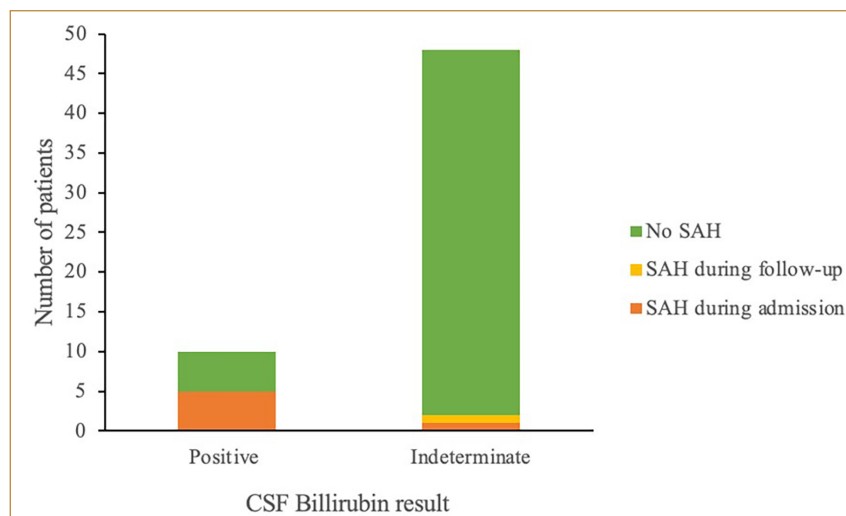


Figure 1. The number of patients with SAH by CSF bilirubin result

CSF results and outcomes:

Of the 677 samples analysed for CSF bilirubin, 619 were negative (91.5%), 48 were reported as indeterminate (7%), and 10 were reported as positive (1.5%) (Figure 1). Of 10 positive CSF bilirubin results, five patients (50%) had a confirmed/suspected SAH, and of 48 indeterminate CSF bilirubin results, just one patient (2.1%) had a confirmed/suspected SAH on discharge.

Outcome of negative CSF bilirubin

No patients with negative CSF bilirubin results developed a SAH during the follow-up period (minimum of 1 year). However, no further analysis of the final diagnosis of the negative CSF results group was undertaken due to the nature of data collection.

Outcome of indeterminate CSF bilirubin

At discharge, only one patient (2.1%) had a diagnosis of SAH in the immediate period following the lumbar puncture; further investigation with CT/MR angiogram identified an aneurysm, and they subsequently underwent inpatient endovascular coiling.

On discharge, 50% (24/48) of those with an indeterminate CSF bilirubin were diagnosed with a primary headache disorder, and 29% (14/48) were diagnosed with a secondary cause of headache, excluding SAH. The electronic records were incomplete for some patients, with no clear diagnosis recorded on discharge for 16.7% (8/48) of the patients with indeterminate CSF bilirubin results (Supplementary Table 1). However, after direct review of electronic patient records, none of these patients were diagnosed with a SAH during the follow-up period.

One patient with an indeterminate CSF bilirubin result was found to have had a SAH during the follow-up period. They had a known posterior

communicating artery aneurysm and were admitted for further investigation following their indeterminate CSF bilirubin result. Inpatient investigations found no evidence of SAH, and so they were discharged for elective, outpatient neurosurgical management. They re-presented with severe headache a few days after discharge and were found to have a SAH on CT, which was successfully treated by embolisation. No other patients had a SAH in the follow-up period (minimum 1 year).

Outcome of positive CSF bilirubin

All patients with positive CSF bilirubin results had a diagnosis recorded at discharge; 20% (2/10) were diagnosed with primary headache disorder, and 20% (2/10) were diagnosed with secondary causes of headache, excluding SAH (Supplementary Table 1). Five patients (50%) had a confirmed/suspected SAH; all underwent CT/MR angiography and cerebral angiograms, which did not show any evidence of an aneurysm requiring intervention. Therefore, all were coded as non-aneurysmal SAH. No patients in this group developed a SAH during the follow-up period.

In our cohort, the number of LPs required to diagnose one aneurysmal or non-aneurysmal SAH was 113 [95% CI 52-303]. The number of LPs needed to diagnose one aneurysmal SAH requiring intervention was 677 [95% CI 0-122].

Timing of investigations:

The median time from ED arrival to CT head scan was 3.03 hours, and the median time from CT head scan to LP was 14.03 hours (Table 1). The median time from the CT head scan to the reported CSF bilirubin result was 19.23 hours. Based on this, and the calculated number needed to diagnose, the number of bed days in the hospital required to diagnose one SAH was 91 days in this cohort.

Most patients arrived in hours corresponding to daytime shifts in the department, with 76.8% (519) arriving between 0900-2100, and 58.6% (319) on weekdays between 0900-2100. CT head scans were performed throughout the day, with 64.7% (432) occurring between 0900-2100. Most LPs were performed on weekdays between 1000-1700, corresponding to better-staffed times in the department. LPs were rarely carried out overnight, with only 4.1% (28/677) of LPs being performed between 0000-0900 (Table 1, Figures 2a and 2b).

Discussion

This service evaluation showed that just 0.9% (6/677) of patients with headache who underwent an LP for CSF bilirubin analysis in the acute medical and ED setting over a four-year period were diagnosed with SAH. This is similar to other studies where the

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Figure 2. Heatmap demonstrating the time and number of patients. Figure 2a corresponds to the time of ED arrival, and Figure 2b corresponds to the time LPs were performed for CSF bilirubin analysis. The heatmaps are based on a colour scale from green to red representing the number of patients in each 1-hour time period (range 1-18) with white representing 0.

prevalence of SAH was 0.65% in patients who had an LP after a negative CT head^{12,13}. Whilst the sensitivity of an LP to diagnose a SAH following a negative CT head can be as high as 100%, there can be a relatively high false positive rate¹². A review of three papers which carried out spectrophotometric CSF analysis reported a pooled false positive rate of 4.8%¹². However, another study reported a false positive rate of 60.7%, which is closer to the false positive rate in our cohort of 50%¹⁴. In our cohort, the false positive rate could be explained by some patients having CSF bilirubin analysis when the history was not in keeping with that of a SAH – i.e. they had a low pre-test probability of SAH. However, a limiting factor here is that we were unable to review the full history and examination findings in our cohort due to the absence of full electronic records. After further neuroimaging, only one patient (0.1%) was diagnosed with an aneurysmal SAH and underwent intervention. This patient had an indeterminate CSF bilirubin result. Therefore, the diagnostic yield of an LP to exclude SAH in the acute medical setting in those with a negative CT head scan is very low. In our cohort, 113 LPs needed to be performed to diagnose one SAH, and 677 LPs to be performed to diagnose one aneurysmal SAH requiring intervention.

The clinical history of those presenting with acute severe headache remains an important aspect of the diagnostic process. However, the use of these signs in clinical decision rules such as the Ottawa SAH is often associated with low specificity (23.7%) and a high false positive rate (76.3%)¹². In contrast, CT head scans have both a high sensitivity (100%) and specificity (100%) when performed within 6 hours¹⁵. Recent studies have

also suggested that modern multislice CT head scans have a high sensitivity (100%) for detection of SAH up to 24 hours^{16,17}. Therefore, greater weight should be placed on objective tests such as neuroimaging to exclude a diagnosis of SAH in a presentation of acute severe headache.

Acute and emergency physicians see many people presenting with acute, severe headache each day. Only a select proportion of these go on to be referred to neurology or neurosurgery. A study in Ireland found that 180/7757 (2.3%) of ED attendances over eight weeks were due to headache. The most common final diagnosis on discharge was migraine for patients discharged directly from the ED without neurology referral (27%), as well as inpatient referrals to the neurology service (86%)¹⁸. This is in keeping with an audit of all attendees to ED over 6 months, which found that 297 (30.4%) of headache presentations had a final diagnosis of migraine. Only 18 (1.8%) of all those with headache presentations had a final diagnosis attributed to a vascular disorder, including SAH; none of these diagnoses were made with an LP².

The acute physician must assess the risks and diagnostic benefits of performing an LP in an individual presenting with an acute severe headache and a negative CT head scan. An LP is an invasive procedure with the potential to cause harm; side effects range from the more common low-pressure headache or back pain to the rarer, such as cerebral herniation or meningitis¹⁹. A study examining the risk-benefit analysis of lumbar puncture found a significantly higher rate of LP-related complications compared to the number of SAH diagnosed ($p < 0.01$); therefore, in a low-risk patient, the risk may outweigh the benefit¹³.

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Possible indications for an LP in those with acute, severe headache to diagnose SAH

- **Patient:**
 - History or examination findings strongly suggestive of SAH.
- **Radiologic:**
 - Negative, or inconclusive, CT scan performed > 6 hours from onset and high clinical suspicion of SAH.
 - CT scan, or reporting, inadequate and unable to rule out SAH.
 - Secondary imaging, such as CTA/MRA inappropriate or unavailable.
- **Other:**
 - No other alternative diagnosis.

Figure 3. Possible indications to perform an LP in people presenting with acute, severe, non-traumatic headache in whom a SAH is suspected. If any of these points are met, it may be appropriate to have a 'diagnostic stop' and review the history, examination findings, and imaging with a senior to determine if an LP is indicated.

Some have suggested that it may be time for secondary neuroimaging (such as CT angiography) to replace LP in patients with suspected SAH^{20,21}. However, others argue that due to the reduced sensitivity of CT head scan after 6 hours, an LP is still required if clinically suspicious of SAH^{12,16}.

Given the number of people with acute, severe, atraumatic headache seen in the ED, it would be inappropriate and unsafe to perform an LP in all. However, in those in whom no other cause of secondary headache is suspected, which may require an LP to diagnose (such as meningitis), there are still some circumstances in which an LP may be considered (*Figure 3*). These factors, alongside others such as whether the correct clinical question was posed when requesting the CT head (i.e. to rule out SAH) and adequate safety netting of the patient, should be considered before omission of an LP²². Future work should look to prospectively evaluate history, examination findings, CT scan results and timing in relation to headache onset and outcome in patients with acute, severe headache to determine whether any other considerations should be made prior to omission of an LP.

In our cohort, LPs were less frequently completed overnight, with only 14.8% occurring between 9 pm and 9 am and 4.1% between midnight and 9 am. It is recommended that an LP should be performed ≥ 12 hours from symptom onset to reduce false negative results¹¹. Our service evaluation demonstrated that the median time from CT head scan to LP was 14 hours. In reality, given the time from symptom onset to CT head scan, virtually all would likely be ≥ 12 hours from symptom onset. However, a limitation of our data is that we did not have reliable data on symptom onset for the entire cohort. Our calculated total number of bed days in hospital required to diagnose one SAH is 91 days. This reiterates the importance of considering whether an LP is indicated in those presenting with acute severe headaches and a negative CT head scan. Our findings suggest that admitting a patient with an acute severe headache and a negative CT head scan to undergo an LP to exclude SAH encumbers a high

resource burden with a low clinical risk. If considered necessary, the LP could be safely completed in a next-day semi-elective setting, leading to an earlier discharge of the patient.

Finally, in patients with acute severe headache in whom objective tests have ruled out a SAH, it is important to re-interrogate the clinical history to aid in the diagnosis of other causes of this presentation. Approximately 30% of those presenting to the ED with headache will be diagnosed with migraine². In our cohort, 25/58 (43.1%) of those with a positive/indeterminate CSF bilirubin result were later diagnosed with a primary headache disorder (*Supplementary Table 1*), and 12/25 (48%) of those underwent further follow-up neuroimaging. There is a need for improved diagnosis and treatment of migraine in the acute medical setting, and improved education among physicians increases the diagnostic accuracy of tension-type headache and migraine²³. It has previously been shown that females have a higher frequency and severity of migraine attacks compared to males^{24,25}. In our cohort, there were significantly more females (60.9%) than males (39.1%) who underwent LP for CSF bilirubin spectrophotometric analysis ($p < 0.0001$). This may reflect sex-based differences in migraine incidence and presentation.

Our service evaluation has several limitations. We are unable to fully exclude the possibility that some patients awaiting an LP in the ED overnight acutely deteriorated prior to it being performed. Therefore, any decision to discharge for a semi-elective LP should be made on a case-by-case basis with senior input and would require appropriate safety-netting advice. The major limitation of this work is the retrospective nature, and therefore, we cannot exclude that some of the CSF samples sent for analysis were obtained when SAH was not a differential diagnosis. Our final cohort only included samples taken in the ED and acute medical setting, which reduces the probability that CSF spectrophotometric analysis was carried out in those in whom SAH was not considered. None of the patients with negative CSF bilirubin results went on to develop a SAH, but we did not collect individualised data on diagnosis at discharge, as this was not the primary focus of this service evaluation. NICE guidelines recommend a CT head scan to be completed within 6 hours of symptom onset¹⁰. Due to the absence of full electronic health records, we were unable to reliably obtain data on the time of symptom onset. Future studies should look at continuing to validate time between symptom onset and CT head scan in the diagnosis of SAH.

Conclusion

In conclusion, we report that the diagnostic yield of CSF bilirubin spectrophotometric analysis in the

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acute medical and ED setting is low in neurologically intact patients with a CT head that does not show any evidence of SAH. Our data challenges the dogma that LP is necessary in all patients with acute severe headache and no evidence of SAH on CT head. We recommend careful evaluation of the indication and clinical need for LP in patients with acute severe headache and a normal CT head scan. We also provide data to demonstrate that LPs are completed with a

lower frequency overnight. Therefore, we recommend that many patients who require an LP to exclude increased CSF bilirubin would be suitable to have the LP completed in a next-day semi-elective setting, thus facilitating an earlier discharge and better use of NHS resources and patient time.

Conflict of interest

none

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Supplementary

Table 3. Diagnosis data for positive and indeterminate results.

Diagnosis	CSF result	Number of patients	Patients undergoing CT/MR angiogram (number of scans showing presence of an aneurysm)	Patients undergoing cerebral angiogram (number of scans showing presence of an aneurysm)	Patients with subsequent neurosurgery or neurology follow-up†
Primary headache disorder					
Migraine	Positive	1	1 (0)	1 (0)	1
	Indeterminate	7	2 (0)	0	2
Cluster headache	Positive	0			
	Indeterminate	1	0	0	0
Primary headache associated with sexual activity	Positive	1	1 (0)	0	0
	Indeterminate	2	1(0)	0	0
Primary stabbing headache	Positive	0			
	Indeterminate	1	1 (0)	0	0
Benign headache, type unspecified	Positive	0			
	Indeterminate	13	7 (1) *	1 (1) †	3
Secondary headache disorder					
Aneurysmal SAH	Positive	0			
	Indeterminate	1	1 (1)	1 (1)	1
Non-aneurysmal SAH	Positive	5	5 (0)	5 (0)	5
	Indeterminate	0			
Stroke/TIA	Positive	0			
	Indeterminate	1	0	0	0
Disorder of sinuses	Positive	0			
	Indeterminate	1	0	0	0
Idiopathic intracranial hypertension	Positive	0			
	Indeterminate	3	1 (0)	0	3
Intracranial infection	Positive	2	0	0	0
	Indeterminate	3	0	0	0
Systemic infection	Positive	0			
	Indeterminate	5	0	0	0
Venous sinus thrombosis	Positive	0			
	Indeterminate	1	0	0	1
Other diagnosis/not recorded					
Drug/alcohol abuse	Positive	1	0	0	0
	Indeterminate	1	0	0	0
None recorded	Positive	0			
	Indeterminate	8	2 (0)	0	2 (0)

*† This patient had a known posterior communicating artery aneurysm. All inpatient investigations were negative for SAH, and the patient was discharged for elective, outpatient management of the aneurysm. They went on to develop a SAH during the follow-up period.