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Is a lumbar puncture necessary? Identifying the need for a LP with a negative CT scan when diagnosing a non-traumatic subarachnoid hemorrhage

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Is a Lumbar Puncture Necessary? Identifying the need for a LP with a Negative CT Scan when Diagnosing a Non-traumatic Subarachnoid Hemorrhage

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Abstract

Objective: To assess the current standard for the detection of non-traumatic subarachnoid hemorrhage (SAH), and evaluate the need for a lumbar puncture with a negative head CT. Is a negative head CT thorough enough to definitively rule out a SAH?

Design: Systematic literature review

Methods: Our research began on the PubMed database using the search terms Subarachnoid Hemorrhage and Lumbar Puncture. We filtered our data with filters including; data in the last ten years, primary research, and full text articles.

Results: Retrospective studies include; Bianchi et al. (2021), Chee et al. (2020) and Tulla et al.(2018). All three studies showed that a negative CT scan less than 24 hours after presenting symptoms is sufficient imaging in detection of a non-traumatic SAH.

Conclusion: There is strong evidence to show that when a patient presents within 24 hours of symptoms suggestive of a SAH, a negative head CT with a third-generation CT scanner is sufficient to rule out a SAH.

Introduction

Subarachnoid hemorrhage (SAH) is a bleed in the subarachnoid space that surrounds the brain, which can be due to a traumatic or non-traumatic cause. The subarachnoid space is part of the 3 layers surrounding the brain: the dura mater, subarachnoid mater, and pia mater. The subarachnoid space lies between the layers of pia mater and arachnoid mater. This can be devastating when blood collects between these layers as it displaces or puts pressure around the brain as well as creates irritation and inflammation of the brain tissue. The most common cause of non-traumatic SAH occurs when a weak bulging blood vessel (aneurysm) on the surface of the brain ruptures.

Due to the limited space around the brain, the accumulating blood causes a rise in the intracranial pressure that will result in devastating complications or death if left undiagnosed. Most patients with a non-traumatic SAH will present with a severe sudden onset headache, often described as "the worst headache of their life," also known as a thunderclap headache.[1] It is estimated that in the United States there are about 10 to 14 per 100,000 people who will have a SAH.[2]

Due to the high morbidity and mortality of a SAH, the current recommendations are that all patients presenting with a severe, rapid onset headache should undergo a workup for a SAH. The current standard of care currently is that if a SAH is suspected the provider should first obtain a CT scan of the individual's brain. If the head CT imaging is negative and there is a high enough clinical suspicion, the next step is to obtain a lumbar puncture and assess for high opening pressure, a raised RBC count, and/or xanthochromia. If these are seen in the cerebral spinal fluid (CSF), it can be diagnostic for a SAH and treatment should be started immediately.[1]

The sensitivity of a negative CT scan within 6 hours of presenting symptoms, read by an experienced radiologist is 100%. Research has shown that the longer time spent between symptom onset and imaging readings shows a decline in the sensitivity.[1] With the advancements

in CT technology it has been questioned whether a negative CT scan within 24 hours is sufficient in ruling out a SAH.

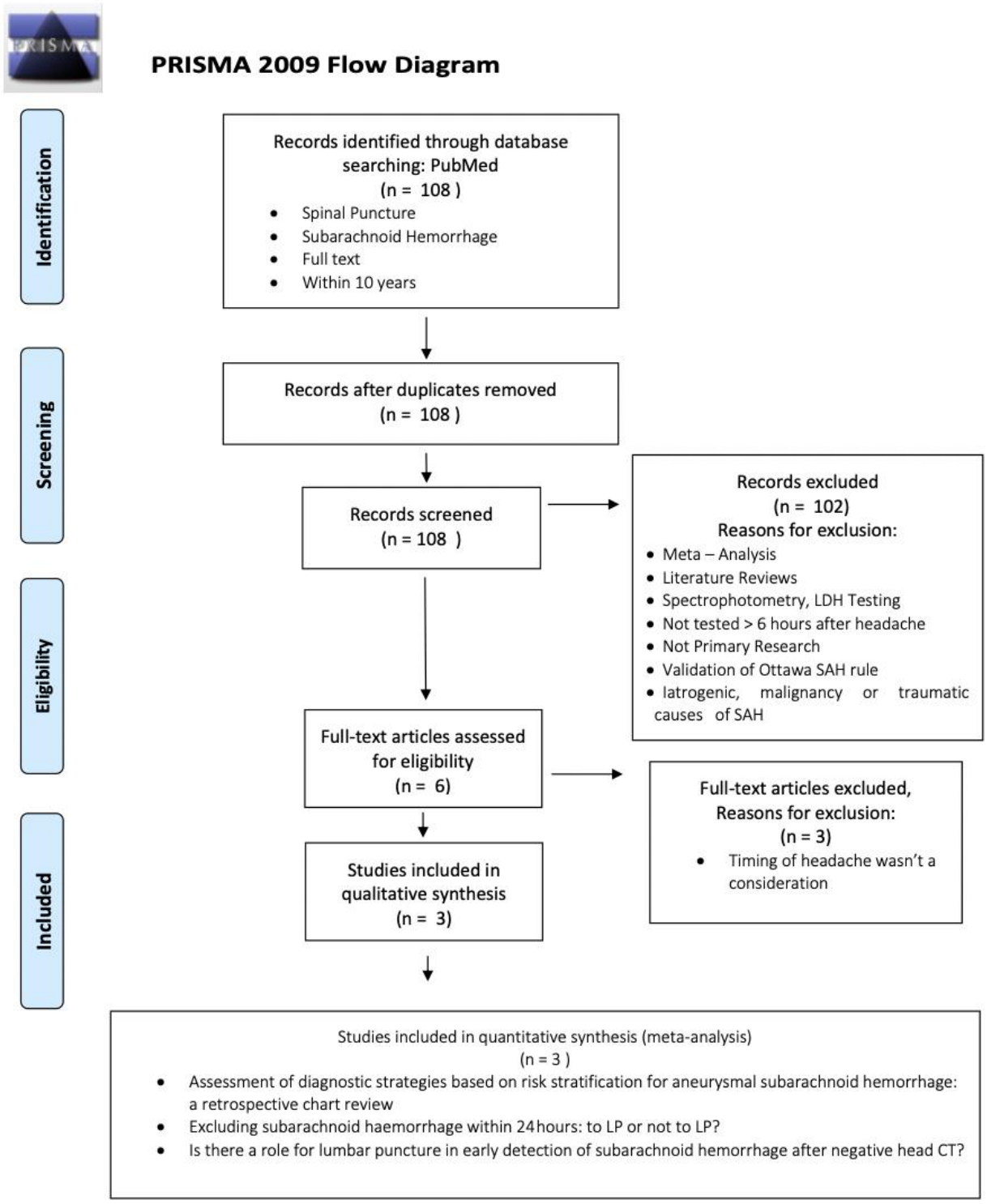
Clinical Question

In patients over the age of 16 presenting with a sudden onset headache suggestive of a subarachnoid hemorrhage (SAH), is getting a negative CT scan within 24 hours as effective in ruling out SAH as compared to getting a lumbar puncture following a negative CT?

Methods

Our initial search began on PubMed, as seen in figure 1, using the search terms "Subarachnoid Hemorrhage," and "Lumbar Puncture." The search yielded 108 results, with zero duplicates. Inclusion criteria included primary research, full text articles, and studies that were published within the last ten years. Reasons for article exclusions included not primary studies, research that was done primarily on CSF analysis or the validation of the Ottawa SAH rule, or if the SAH was due to iatrogenic, malignant or traumatic causes. After our initial screen we found 6 full text articles that examined the role of lumbar puncture after a negative head CT. We further excluded 3 of the articles due to the fact that the time of initial head CT from symptom onset was not examined. This left us with 3 articles that studied the necessity of a lumbar puncture to rule out a SAH following a negative head CT performed within 24 hours of symptom onset. See Figure 1 for the PRISMA flow diagram.

Figure 1: PRISMA Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Results

Study 1

Assessment of diagnostic strategies based on risk stratification for aneurysmal subarachnoid hemorrhage: a retrospective chart review. Bianchi et al. (2021)[3]

Study Objective

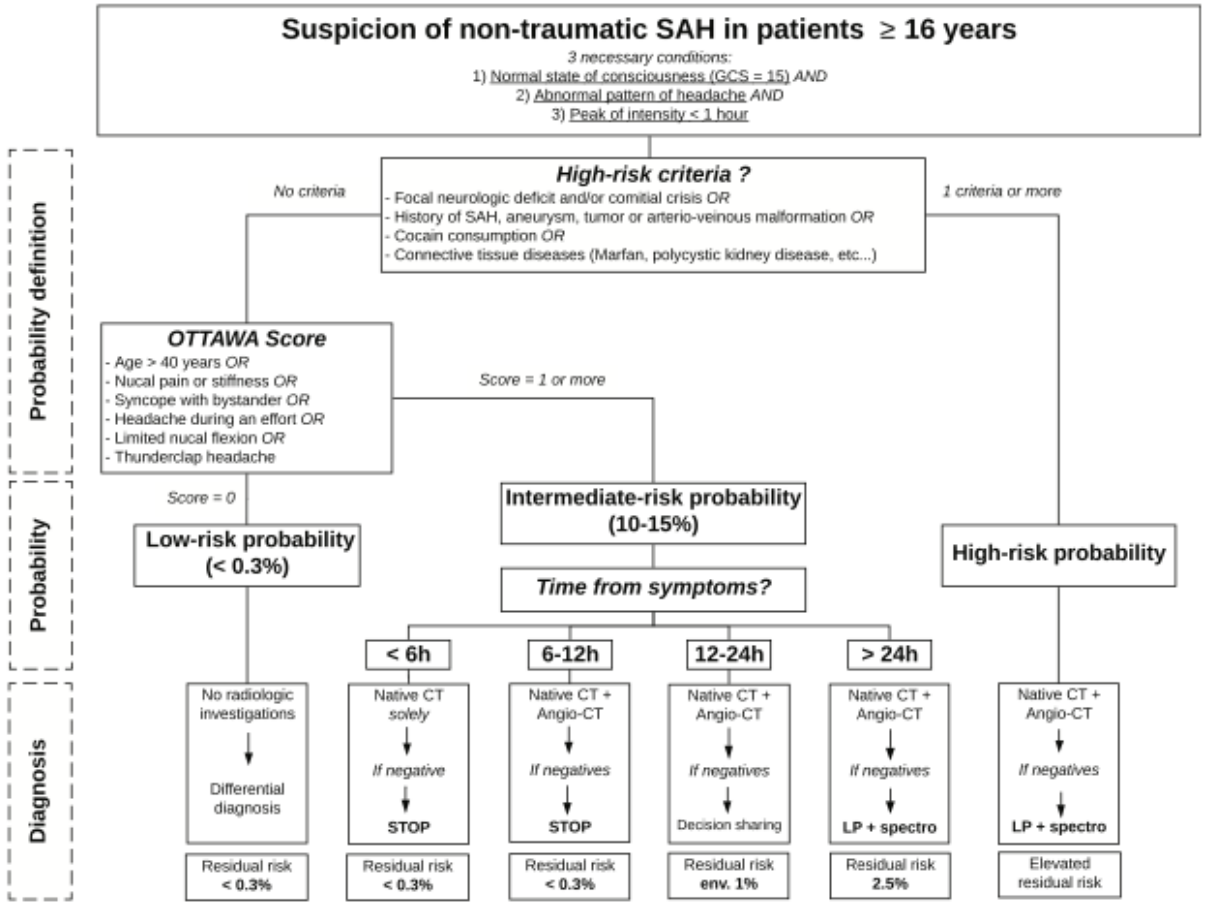
The aim of this study was to evaluate alternative strategies to the current guidelines for suspicion of a SAH. This was done by using a clinical risk stratification comparing the current guideline, which is a non-contrast Computed Tomography (NCCT) and a lumbar puncture if the CT is negative. The alternative strategies that were utilized were a NCCT + Computed Tomography Angiography (CTA) ± lumbar puncture if high clinical risk or negative CT and onset of headache ≥12 hours and ≥24 hours.

Study Design

This was a single-site, retrospective cross-sectional study at the Emergency Department of a university-affiliated, tertiary referral hospital in Switzerland. Patients who presented with an acute headache and a SAH suspicion whose clinical assessment included a NCCT, CTA and lumbar puncture were included in the study. Patient data was collected from 2011 to 1016. The researchers took the results of each investigation (NCCT, CTA and lumbar puncture) and combined them with a clinical risk assessment, including the use of Ottawa score. See figure 2 below for Ottawa score criteria. The inclusion data that was chosen for this study included non-trauma patients that were >16 years old, had a Glascow coma score of 15, and had an abnormal headache, with peak intensity <1 hour. Each patient was put through a stratification assessment and ranked low, intermediate, or high risk of SAH (see figure 2). The patients were then tested using strategy 1 (current guidelines), strategy 2 (NCCTA + CTA in all patients, lumbar puncture in high risk or intermediate risk patients with a negative CT and onset of headache within 12 hours), or strategy 3 (NCCTA + CTA in all patients, lumbar puncture if high risk or intermediate patients with a negative CT and onset of headache within 24 hours). These strategies were retrospectively applied to assess the algorithm (see figure 2).

There were 506 patients with a suspected SAH that were screened, 196 that were excluded for altered mental status, a usual headache, or onset >1 hour. Of the 310 that met criteria, 8 were found to have a SAH. The major outcome observed was diagnosis of SAH at hospital discharge. Other outcomes were death from all causes and need for invasive procedures at 28 days. They used sensitivity, specificity, positive predictive value and negative predictive value (NPV) to evaluate the diagnostic performance of the three strategies.

Figure 2: Risk Assessment Tool[3]



Local protocol for investigation of a suspected aneurysmal subarachnoid hemorrhage (SAH).

Source: Bianchi C, Ageron F-X, Carron P-N. Assessment of diagnostic strategies based on risk stratification for aneurysmal subarachnoid hemorrhage: A retrospective chart review. *European Journal of Emergency Medicine*. 2021;28(5):355-362. doi:10.1097/mej.0000000000000804

Study Results

A NCCT was performed on all patients, and a SAH was detected in 4 of those patients. Lumbar puncture was performed on all patients and 10 patients were found to have xanthochromia. Of these lumbar punctures, 3 were false positives and 1 was a false negative. CTA was performed on 303 patients, and 23 cerebral aneurysms were found. NCCT and CTA both had 1 false negative. All three strategies were found to have high sensitivity and specificity. The sensitivity for the current guidelines was much lower and the difference between the strategies is statistically significant as seen below in figure 3. All tests were read and interpreted by a senior general radiologist and if needed, a neuroradiologist.

The current guidelines have the lowest sensitivity of the three strategies assessed. Strategy 2 and 3 both proved to have 100% sensitivity and 99.7% specificity. Strategies 2 and 3 allowed for 173 lumbar punctures to be avoided, which is a 57% relative reduction in the amount of lumbar puncture procedures performed. Using the risk stratification system as well as a CTA

and CT seems to be the most effective approach to diagnosing a SAH and minimizing the need for unnecessary lumbar puncture within a 24 hour time frame from the onset of the headache.

Figure 3: Performance of the different investigative strategies[3]

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR + (95% CI)	LR- (95% CI)
Strategy 1 (NCCT + lumbar puncture)	87.5 (47.3–99.7)	99.0 (97.1–99.8)	70 (34.8–93.3)	99.7 (98.2–100)	88.1 (27.7–280)	0.126 (0.02–0.79)
Strategy 2 (lumbar puncture if >12 h)	100 (63.1–100)	99.7 (98.2–100)	88.9 (52–99.7)	100 (98.8–100)	300 (42.4–2123)	<0.001 (0–0)
Strategy 3 (lumbar puncture if >24 h)	100 (63.1–100)	99.7 (98.2–100)	88.9 (51.8–99.7)	100 (98.8–100)	300 (42.4–2123)	<0.001 (0–0)

LR+, positive likelihood ratio; LR-, negative likelihood ratio; NCCT, non-contrast computed tomography; NPV, negative predictive value; PPV, positive predictive value.

Source: Bianchi C, Ageron F-X, Carron P-N. Assessment of diagnostic strategies based on risk stratification for aneurysmal subarachnoid hemorrhage: A retrospective chart review. *European Journal of Emergency Medicine.* 2021;28(5):355-362. doi:10.1097/mej.0000000000000804

Study Critique

This study has several strengths, including the design, its methods and organization of data. The researchers had access to a single hospital database that has around 65,000 admissions yearly. This means that the data collected was from a single source, a single EMR, which means that the data sorted through can be more reliably compared. The methods and design seem to be very thorough and provide excellent inclusion and exclusion criteria to minimize bias and variables in outcome. The weaknesses included a smaller than desired sample size for the study. The authors wanted many more patients and data to compare. There could have been less exclusionary criteria (peak intensity less than one hour, altered mental status or a usual headache) which would have included more individuals in the study increasing the sample size. Another possibly problematic variable is that not every CT was analyzed by a radiologist *and* neuroradiologist, which could lead to some misclassifications.

Study 2

Excluding subarachnoid hemorrhage within 24 hours: to LP or not to LP? Chee C et al. (2020)[4]

Study Objective

The aim of this study was to investigate the necessity of a lumbar puncture following a negative head computed tomography for ruling out subarachnoid hemorrhage within 24 hours of symptom onset.

Study Design

This study was a retrospective review of patient records from March 2012 to February 2015. Data was obtained from Nottingham University Hospitals (NUH) National Health Service (NHS) Trust databases. All patients, 17 years and older, who presented with a clinical suspicion of a non-traumatic subarachnoid hemorrhage who underwent both a non-contrast head CT followed by a lumbar puncture for cerebrospinal fluid with xanthochromia were included in the study. Inclusion and exclusion criteria can be seen in figure 4. All patient data was organized based on specific characteristics such as age, gender, symptoms at onset, and time of CT from

onset of symptoms. Patients were diagnosed with a SAH if head CT showed evidence of blood in the subarachnoid space, aneurysm identified on further imaging, or xanthochromia in CSF analyzed via spectrophotometry. The predictive value of a normal head CT to exclude the diagnosis of a SAH was determined.

Figure 4: Inclusion and Exclusion study criteria[4]

Inclusion	Exclusion
- >16 years of age - presented to Nottingham University hospital Emergency departments and acute medical units. - presented with acute non-traumatic headaches	- Traumatic SAH - MRI head as initial imaging modality - Had CSF xanthochromia without initial head CT - CSF xanthochromia requested for conditions not for SAH - Already an inpatient during symptom onset - Transfer from other hospital

Study Results

A total of 1884 patients were identified from the laboratory and clinical databases, of which 999 met inclusion criteria for the study. Out of the 999, 176 were diagnosed with a SAH after a positive head CT. The remaining 823 underwent lumbar punctures, following a head CT negative for SAH. Depending on the lumbar puncture results patients were either discharged or underwent further imaging. Out of the 823 patients who underwent lumbar punctures, 3 were diagnosed with an SAH but only after further imaging was conducted due to inconclusive lumbar punctures. The sensitivity of a head CT to rule out a SAH was calculated and stratified by timing of scan from onset. A normal head CT was observed in those who presented within 6 hours from onset of symptoms (sensitivity of 100% [95% CI 93.9–100]). This high sensitivity persisted up to 24 hours from onset of symptoms but fell to a sensitivity of 94.5 (95% CI 86.6–98.5) once beyond 24 hours (figure 5).

This study suggests that the new generation CT scans are sensitive enough to rule out a SAH if completed within 24 hours of symptom onset and read by an experienced neuroradiologist. This data encourages a shift away from routine lumbar punctures to exclude SAH after a normal head CT is performed within the reasonable time frame.

Figure 5: Test characteristics of head CT in patients with clinical suspicion of non-traumatic SAH stratified by timing of scan from onset of symptoms[4]

Time from ictus to head CT	No. of patients	% Sensitivity (95% CI)	% Specificity (95% CI)	Likelihood ratio (95% CI)		% Predictive value (95% CI)	
				Positive	Negative	Positive	Negative
<6 hours	203	100 (93.9–100)	100 (97.5–100)	Infinity	0.00	100 (92.0–100)	100 (96.8–100)
6–24 hours	213	100 (92.5–100)	100 (97.8–100)	Infinity	0.00	100 (90.6–100)	100 (97.2–100)
>24 hours	583	94.5 (86.6–98.5)	99.8 (98.9–100)	482.1 (67.9–3418.4)	0.05 (0.02–0.14)	98.6 (90.7–99.8)	99.0 (97.8–99.6)
All patients	999	97.2 (93.6–99.1)	99.9 (99.3–100)	796.3 (112.3–5649.7)	0.03 (0.01–0.07)	99.4 (96.1–99.9)	99.4 (98.6–99.7)

Source: Chee C, Roji AM, Lorde N, et al. Excluding subarachnoid haemorrhage within 24 hours: To LP or not to LP? *British Journal of Neurosurgery*. 2020;35(2):203-208. doi:10.1080/02688697.2020.1781055

Study Critique

A few strengths of this study include a large sample size, and that the UK has national guidelines for detecting xanthochromia using spectrophotometry. Other countries, including the United States, use visual inspection with the naked eye as the method of choice in detecting xanthochromia[5].

Similar to all retrospective studies there is a limitation to the accuracy of the data: the timing of initial head CT from symptom onset was estimated from the patient's charts and physician notes. The exact time from symptom onset and head CT was not documented on all patient charts.

Study 3

Is there a role for lumbar puncture in early detection of subarachnoid hemorrhage after negative head CT? Tulla M et al. (2018)[6]

Study Objective

To investigate the role of lumbar puncture after a negative head computed tomography when ruling out subarachnoid hemorrhage within 24 hours of symptom onset.

Study Design

This study was a retrospective cohort study performed in a single center, on a consecutive series of patients from 2011 to 2015. All patients underwent CT (with a third generation CT scanner) or CT followed by lumbar puncture to rule out SAH. The patients were chosen from two electronic medical record databases. All patients who presented to the Emergency Department between January 1st 2011- December 31st 2015, who had a lumbar puncture performed because of a suspicion of SAH were included in the study. Patients were excluded if they refused a lumbar puncture, if a lumbar puncture was performed for other reasons, or they didn't undergo CT imaging. All patients included in the study had a CT scan (3rd generation CT scan) and a lumbar puncture performed. Patients were then categorized into four groups based on the time of symptom onset to initial head CT: up to 6 hours, up to 12 hours, up to 24 hours, and over 24 hours.

Study Results

Over this 5-year study, a total of 647 patients were suspected of having a SAH and were included in the study. All 647 patients were treated based on current guidelines, receiving an initial head CT, followed by a lumbar puncture if head CT was negative for SAH. Out of the 647 patients, 108 patients were diagnosed with a SAH through the initial head CT. The remaining 539 patients underwent a subsequent lumbar puncture due to a negative head CT. The initial head CT was performed within 6 hours in 132 patients, 6–12 hours in 99 patients, 12–24 hours in 49, and over 24 hours from symptom onset in 259 patients. Only 5 patients had a positive lumbar puncture for SAH after a negative head CT, and all 5 patients received their initial head CT 24 hours after symptom onset. The sensitivity of a head CT performed within 24 hours of symptom

onset was 100% (95% CI 95–100%). This data supports the theory that there is no added benefit from performing an lumbar puncture after a negative head CT, performed within 24 hours of symptom onset, in ruling out a SAH. After 24 hours of symptom onset CT was not sufficient in ruling out SAH, and thus lumbar puncture is still recommended in clinical practice, although other modalities (i.e., CTA/MRA) may be useful for further evaluation.

Study Critique

The strengths in this study include its sample size. This study has a bigger sample size than in the first study we looked at, and is more comparable in size to the second study. There are a few weaknesses in this study, the most concerning is likely the quality of the record keeping in some patients. Most patients had good documentation, but there were some patients who had lumbar punctures performed and it was not specifically noted why from the clinician. So there may have been patients that had their data included when there wasn't a concern for SAH, which could skew the data. The study also did not include patients that received a head CT with a negative result, but not a lumbar puncture. The authors acknowledge that a prospective study design could overcome some of these limitations presented.

Discussion:

Subarachnoid hemorrhage (SAH) is a life-threatening condition that if left undiagnosed can result in devastating neurologic complications or death. Due to the importance of accurate detection current recommendations include a non-contrast head CT followed by a lumbar puncture. Current standard for detecting a SAH with a non-contrast CT is highest within the first six hours of symptom onset. Newer research suggests that the sensitivity of CT when performed within 24 hours of symptom onset is sufficiently sensitive making a follow-up lumbar puncture unnecessary. The purpose of this review was to determine if getting a negative CT scan within 24 hours of symptom onset sufficient for ruling out a SAH, and therefore making a follow up lumbar puncture unnecessary.

Study	Bianchi et al.	Chee et al.	Tulla et al.
Patients, N	N = 310	N = 999	N = 539
Population	Patients >16 yo presenting with symptoms suggestive of non-traumatic SAH	Patients >17 yo presenting with a clinical suspicion of a non-traumatic subarachnoid hemorrhage	Patients 17-96 yo presenting with symptoms suggestive of non-traumatic SAH
Primary interest	Detection of Subarachnoid hemorrhage	Detection of Subarachnoid hemorrhage	Detection of Subarachnoid hemorrhage

Patient Categorization	Risk Stratification: Low, intermediate or high probability of SAH based on presentation and symptoms	Time of symptom onset to initial head CT 1. <6 h 2. 6-24 h 3. >24 h 4. All patients	Time of symptom onset to initial head CT 1. <6h 2. 6-12 h 3. 12-24 h 4. >24 h
Intervention	All patients underwent a head CT followed by a lumbar puncture if CT was negative 1. NCCT + LP (<6 hrs.) 2. NCCT + CTA + LP (≥12 h) 3. NCCT + CTA + LP (≥24 h)	All patients underwent a head CT followed by a lumbar puncture if CT was negative Patients with positive LP got a CTA or MRA or IADSA	All patients underwent a head CT followed by a lumbar puncture + CTA or + MRA or + DSA (if negative CT)
Sensitivity (95% CI) of CT for detection of SAH <24 hours of symptom onset	1. 87.5% (47.3-99.7) 2. 100% (63.1-100) 3. 100% (63.1-100)	1. <6 h - 100% (93.9-100) 2. 6-24 h - 100% (92.5-100) 3. >24 h - 94.5% (86.6-98.5) 4. All patients - 97.2% (93.6-99.1)	<24 h- 100% (95-100) All patients- 95% (89-98)

Table 1: Table comparison and overview of the three studies reviewed

An overview of the three studies can be seen above in table 2. All of the studies reviewed followed the standard of care of a lumbar puncture following a negative head CT. Even though Bianchi et al. study had the smallest population size, they had the most organized approach by using a risk stratification and identifying the approach for each patient's clinical workup. It was easiest to understand their clinical reasoning and diagnostic approach to each patient. This provides strength in the data collected, as it specifically highlights that the time frame of symptoms onset should not be the only consideration when determining the necessity of an lumbar puncture. A limitation of this study was that not all patients underwent the same diagnostic workup. This makes the reader question whether the increase in sensitivity is due to the improvement of CT technology or the addition of contrast to the head CT.

Chee et al. and Tulla et al. were very similar in their data collection, and patient criteria. Both studies included all patients presenting with symptoms suggestive of SAH whose diagnostic workup included both a lumbar puncture following a negative non-contrast head CT. Chee et al. study included the largest sample size and organized all patients into data sets based on time of symptom onset to initial head CT. Similar to the other studies they found that the sensitivity of a non-contrast head CT lessens dramatically after 24 hours of symptom onset. Similar to study 2, Ziu E et al., study 3, Tulla et al., also organized their patients into categories based on time of symptom onset to initial head CT. Even though the patients were placed into these categories, they did not provide sensitivity for all 4 groups. Although the data show a sensitivity of 100% if a head CT is done within 24 hours, having the specific data and confidence intervals for each group would be beneficial in identifying if there is a more sensitive approach.

A major limitation of all three studies and all data collected for diagnosing a subarachnoid hemorrhage is the fact that all data has to be retrospectively collected. Due to the ethical limitations, randomized control trials would be almost impossible to design. Due to the retrospective nature of the data collection there are questions that are unable to be answered, such as why some patients underwent further imaging modalities and others did not. It may even be seen as a confounding variable, due to the fact that some of the patients were diagnosed based on additional imaging. Another limitation in retrospective studies is that the diagnostic approach of each clinician can only be assumed from charting, which was not always indicated. In Bianchi et al. they have a clear and organized approach in their diagnostic work-up in each patient, which was not as clear in the Chee et al. and Tulla et al. studies.

Conclusion:

In patients over the age of 18 presenting with a sudden onset headache suggestive of a nontraumatic subarachnoid hemorrhage (SAH), is getting a negative CT scan within 24 hours as effective in ruling out SAH as compared to getting a lumbar puncture following a negative CT?

There is strong evidence to show that when patients with symptoms indicative of a SAH present and undergo head CT within 24 hours of symptom onset, with a 3rd generation CT. scanner, the imaging should be sufficient in ruling out a SAH in patients. The data also showed that there is diagnostic value in including a CTA to the diagnostic workup.

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