SPECIAL CONTRIBUTION

Can Computed Tomography Angiography of the Brain Replace Lumbar Puncture in the Evaluation of Acute-onset Headache After a Negative Noncontrast Cranial Computed Tomography Scan?

Robert F. McCormack, MD, and Alan Hutson, PhD

Abstract

Objectives: The primary goal of evaluation for acute-onset headache is to exclude aneurysmal subarachnoid hemorrhage (SAH). Noncontrast cranial computed tomography (CT), followed by lumbar puncture (LP) if the CT is negative, is the current standard of care. Computed tomography angiography (CTA) of the brain has become more available and more sensitive for the detection of cerebral aneurysms. This study addresses the role of CT/CTA versus CT/LP in the diagnostic workup of acute-onset headache.

Methods: This article reviews the recent literature for the prevalence of SAH in emergency department (ED) headache patients, the sensitivity of CT for diagnosing acute SAH, and the sensitivity and specificity of CTA for cerebral aneurysms. An equivalence study comparing CT/LP and CT/CTA would require 3,000 + subjects. As an alternative, the authors constructed a mathematical probability model to determine the posttest probability of excluding aneurysmal or arterial venous malformation (AVM) SAH with a CT/CTA strategy.

Results: SAH prevalence in ED headache patients was conservatively estimated at 15%. Representative studies reported CT sensitivity for SAH to be 91% (95% confidence interval [CI] = 82% to 97%) and sensitivity of CTA for aneurysm to be 97.9% (95% CI = 88.9% to 99.9%). Based on these data, the posttest probability of excluding aneurysmal SAH after a negative CT/CTA was 99.43% (95% CI = 98.86% to 99.81%).

Conclusions: CT followed by CTA can exclude SAH with a greater than 99% posttest probability. In ED patients complaining of acute-onset headache without significant SAH risk factors, CT/CTA may offer a less invasive and more specific diagnostic paradigm. If one chooses to offer LP after CT/CTA, informed consent for LP should put the pretest risk of a missed aneurysmal SAH at less than 1%.

ACADEMIC EMERGENCY MEDICINE 2010; 17:444–451 © 2010 by the Society for Academic Emergency Medicine

Keywords: subarachnoid hemorrhage, acute onset headache, computed tomography, computed tomography angiography, lumbar puncture, diagnosis

Headache is a frequent complaint in the emergency department (ED). When a patient complains of an acute-onset headache, the possibility of a subarachnoid hemorrhage (SAH) must be entertained. The standard diagnostic strategy to exclude a SAH is a noncontrast cranial computed tomography (CT), followed by lumbar puncture (LP) if the initial CT scan is negative. This diagnostic strategy has recently been validated in a study by Perry et al. CT scan followed by LP shows a sensitivity of 100% and negative predictive value of 100% in excluding SAH. However, LP is invasive and time-consuming. It can be technically difficult due to body habitus, poor patient cooperation, and patient anxiety. Postdural puncture headache occurs in up to 40% of patients and can add to suffering. There is significant controversy regarding what constitutes a positive tap versus a traumatic tap. An "equivocal" LP occurs 15% to 20% of the time and often mandates further workup. Recent advances and availability of...
computed tomography angiography (CTA) raise the possibility of an alternative diagnostic strategy. Can CTA replace LP after a negative CT to exclude SAH due to aneurysm or arterial venous malformation (AVM)?

It is difficult to prove that these are equivalent diagnostic strategies because of the strength of the initial diagnostic test (CT) and a near zero margin for error in diagnosis. It is well established in the literature that patients who suffer a missed diagnosis of SAH do poorly.5–7 A missed diagnosis is more likely to occur with subjective presentations and often results in death or permanent disability. In those patients where the “sentinel” hemorrhage is detected, the outcome is much more favorable. Because of this opportunity to greatly influence overall outcomes, it is clinically imperative to find all patients with SAH due to an aneurysm.

Approximately 85% of SAH are due to aneurysm or AVM.8–11 SAHs that are not due to cerebral aneurysm or AVM tend to have better prognoses.12 Approximately 10% will display a perimesencephalic pattern of bleeding and carry a good prognosis.13 The small remainder will be due to vasculitis, tumors, coagulation disorders, and a variety of other causes and typically carry a better prognosis than those caused by aneurysms.9,14 Aneurysms without SAH are often undetected in the current standard of care. A “symptomatic aneurysm” without actual hemorrhage has been postulated as a cause of acute-onset headache. However, on long-term follow-up with the current diagnostic strategy, those patients who do not have SAH but may have an aneurysm even in the presence of acute headache do well.1,15–19

The cases a physician cannot afford to miss are those with both SAH and an aneurysm or AVM present. Missing either diagnosis alone when the other diagnosis is not present is not optimal, but should be relatively acceptable due to a better prognosis. CT is sensitive for SAH, and CTA is very sensitive for aneurysm, but both remain less than perfect. However, the performance of the two tests is additive when the goal is to exclude the concurrent presence of both diseases. We constructed a mathematical model to assess the posttest probability of both SAH and aneurysm being present when both CT and CTA are negative. We hypothesize that in select patients, CT/CTA can replace CT/LP as a diagnostic strategy for aneurysmal SAH.

**METHODS**

After a MEDLINE search (key words: subarachnoid hemorrhage, tomography x-ray computed, spinal puncture, angiography, angiography digital subtraction; from 1996 to present) and review of article references, we selected the most recent and relevant studies with regard to SAH prevalence in ED patients complaining of acute-onset headache, the sensitivity of CT for the diagnosis of SAH, and the sensitivity and specificity of CTA for cerebral aneurysm.

**SAH Prevalence**

There is no published meta-analysis of SAH prevalence in ED patients with an acute-onset headache and a normal neurologic exam. Based on the current literature, the prevalence is between 3% and 16% (Table 1).1,19–22 We have conservatively estimated the prevalence of SAH in an ED patient complaining of an acute-onset headache with an intact neurologic exam as 15%. Although the actual prevalence may be lower, assuming a higher prevalence in a probability model will maximize the number of potential missed cases and reveal weaknesses in the model.

Patients with acute-onset headache and abnormal mental status or neurologic deficits are presumed to have a higher prevalence of SAH. Currently, there are no adequate prevalence data for SAH in this subgroup of patients and therefore they should not be included in this model.

**CT Sensitivity**

A noncontrast cranial CT has a sensitivity for SAH between 82% and 100%, depending on the timing of the study after the onset of the headache (Table 2).20,23–27 The 95% confidence intervals (CIs) substantially lower these sensitivities. Most clinicians estimate the sensitivity to be above 90% in the first 24 to 48 hours after headache onset. Sensitivity continues to decrease with time due to diffusion of blood away from the site of hemorrhage. The studies on sensitivity of CT scan are limited by selection bias, retrospective design, and the challenge of keeping pace with advancements in technology. There is no published meta-analysis. Comparison of the results shows performance to be similar between studies. We have selected the publication by Byyny et al.20 as a representative study for the purpose...

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**Table 1**

Selected Studies Reporting Prevalence of SAH in ED Headache Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Data</th>
<th>Prevalence</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bo et al.22</td>
<td>433 patients/71 SAH</td>
<td>16%</td>
<td>Norway, majority referred by GPs, possible selection bias</td>
</tr>
<tr>
<td>Perry et al.1</td>
<td>592 patients/61 SAH</td>
<td>10%</td>
<td>CT/LP verification study</td>
</tr>
<tr>
<td>Carstairs et al.21</td>
<td>116 patients/5 SAH or aneurysm</td>
<td>4.3%</td>
<td>CT/CTA for aneurysm or SAH</td>
</tr>
<tr>
<td>Boesiger and Shiber20</td>
<td>116 patients/3 SAH</td>
<td>2.5%</td>
<td>Retrospective, found pt by LP/CT/CTA for aneurysm or SAH</td>
</tr>
<tr>
<td>Landblom et al.19</td>
<td>177 patients/6 SAH</td>
<td>3.4%</td>
<td>Sweden, University ED</td>
</tr>
<tr>
<td>Lander et al.18</td>
<td>137 patients/23 SAH</td>
<td>11.3%</td>
<td></td>
</tr>
</tbody>
</table>

CT = computed tomography; CTA = computed tomography angiography; dx = diagnosis; GP = general practitioner; LP = lumbar puncture; SAH = subarachnoid hemorrhage.
of our model because it best represents ED headache patients with acute-onset headache and normal neurologic exam. The study by Lourenco et al.27 study was excluded because it allowed altered mental status and neurologic abnormalities, which could skew test sensitivity. The study by Boesiger and Shiber20 was excluded because of the wide CIs due to study size and design. The studies by Sidman et al.,24 Sames et al.,25 and van der Wee et al.23 were felt to use outdated CT technology and are limited by patient selection bias. The specificity of CT for SAH is not reported in most studies, but is assumed to be 100%.

LP Sensitivity
LP shows excellent sensitivity. The recent study by Perry et al.1 demonstrates 100% sensitivity. However, the specificity is low, at 67%.

CTA Sensitivity
Numerous studies have examined the performance of CTA for aneurysms in the setting of SAH. CTA has been shown to be a reliable substitute for the traditional criterion standard of digital subtraction angiography (DSA) for aneurysm diagnosis in a number of recent studies. Sixty-four-detector CTA of the brain has been shown to be 98% sensitive and 100% specific for the detection of aneurysms in the setting of SAH.28

Multiple other studies of 16-, four-, and single-detector CTA indicate similar sensitivities and specificities (see Table 3).28–32 All of these studies include patients with variable levels of mental status and neurologic exam findings who have a diagnosis of SAH by CT or LP. We selected the study by Agid et al.28 because it utilized 64-detector technology. There is no formal published meta-analysis, and the most recent review in the literature is now technologically obsolete.

It would be very difficult to prove a new diagnostic strategy that could match the sensitivity of the current CT/LP strategy. Because of the low prevalence of disease and excellent sensitivity of the initial study, large numbers of patients would be needed to prove that CT/CTA is equivalent to CT/LP. For example, assume that the CT/LP strategy has a sensitivity of 99.9%. If a study were to compare the sensitivity rates in a randomized two-arm equivalence trial of CT/LP versus CT/CTA, and assuming equivalence is defined as a one-sided 0.5% window within the target sensitivity of 99.9% (i.e., within the range of 99.4%–99.9%), then roughly 3,000 subjects would need to be accrued to the respective trial. Due to the low prevalence of disease, it would take significant time and resources to conduct a study with sufficient power. The only study on SAH in ED patients to enroll 3,000 patients took 8 years and 12 centers to accrue.23 Note that a more refined sample size calculation would depend on the respective investigator’s specific set of input parameters.

RESULTS
Patients who present to an ED with a chief complaint of acute-onset headache and have an intact neurologic exam have a conservatively estimated pretest probability of SAH of 15%. Patients with loss of consciousness associated with acute headache, those with menignismus or cranial nerve findings, or those with significant risk factors (first-degree relative with aneurysm, connective tissue disease, polycystic kidney disease) may have a higher pretest probability that has not been adequately defined and should be included from this model.

Review of the literature on CT for SAH shows fairly consistent results over the past 15 years. The study by Byyny et al.26 showed sensitivity of 91% with a 95% CI = 82% to 97% and a specificity of 100% in neurologically intact patients with an acute-onset headache. CT sensitivity is well known to diminish with prolonged time from ictus. For the purpose of this model, time from ictus to CT should be less than 48 hours.

The sensitivity and specificity of CTA for diagnosis of cerebral aneurysm in the setting of SAH have been remarkably consistent with multidetector CT. Agid et al.28

<table>
<thead>
<tr>
<th>Study</th>
<th>Data</th>
<th>Sensitivity, % (95% CI)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lourenco et al.27</td>
<td>61 SAH:</td>
<td>97 (84–100)</td>
<td>Did not factor time to CT, retrospective, allowed abnormal mental status and exam</td>
</tr>
<tr>
<td></td>
<td>60 CT, 1 LP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Byyny et al.26</td>
<td>149 SAH:</td>
<td>93 (88–97)</td>
<td>Did not factor time to CT, retrospective, subgroup of HA</td>
</tr>
<tr>
<td></td>
<td>HA, normal exam</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>139 CT, 10 LP</td>
<td>91 (82–97)</td>
<td>with normal neuro exam</td>
</tr>
<tr>
<td>Boesiger et al.20</td>
<td>177pts/6 SAH:</td>
<td>100 (84–100)</td>
<td>Did not factor time to CT, wide CI, retrospective</td>
</tr>
<tr>
<td></td>
<td>6 CT, 0 LP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sidman et al.24</td>
<td>140 patients</td>
<td>Overall 92</td>
<td>Retrospective, 100% prevalence, allowed abnormal mental status/exam</td>
</tr>
<tr>
<td></td>
<td>80/80 CT &lt;12 hours</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49/60 CT &gt;12 hours</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>Sames et al.25</td>
<td>114 &lt; 24 hours HA</td>
<td>93</td>
<td>Retrospective, 100% prevalence, allowed abnormal mental status/exam</td>
</tr>
<tr>
<td></td>
<td>37 &gt; 24 hours HA</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Van der Waal et al.23</td>
<td>175 patients 119 SAH:</td>
<td>98</td>
<td>CT &lt;12 hours, high prevalence (69%) of disease</td>
</tr>
<tr>
<td></td>
<td>117 CT, 2 LP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT = computed tomography; HA = headache; LP = lumbar puncture; SAH = subarachnoid hemorrhage.
demonstrated CTA sensitivity for aneurysm was 97.9% with a 95% CI = 88.9% to 99.9%, and specificity was 100%. This study group is different than our target group in that all of these patients had SAH and varying clinical presentations. We are looking for aneurysms in patients with or without SAH. However, we will never be able to obtain true sensitivity and specificity of CTA in this patient setting because it would be impractical to conduct CTA and DSA testing on ED headache patients in the patient setting because it would be impractical to conduct CTA and DSA testing on ED headache patients in the absence of SAH. Eighty-five percent of SAHs are caused by aneurysms or AVM. We assume a baseline prevalence of aneurysm without SAH as 2.5% based on the literature (Table 4).34–36

Computed tomography looks for blood in the subarachnoid space. CTA looks for cerebral aneurysms. Assuming that these two tests are independent of one another, the expected proportion of cases falling into a particular diagnostic category can be calculated as a function of the joint probability of each test being either positive (+) or negative (−) times the respective sensitivity (+|+) or 1 − sensitivity (−|+) and specificity (−|−) or 1 − specificity (+|−) depending on the +/- test combinations.

Table 3
Selected Studies Reporting Sensitivity of Multidetector CTA for Cerebral Aneurysm

<table>
<thead>
<tr>
<th>Study</th>
<th>Data</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kokkinis et al.32</td>
<td>198 patients SAH: 179 w/ AN, 15 AVM</td>
<td>97.9</td>
<td>100</td>
<td>Single detector, found all AVMs 16-detector CT</td>
</tr>
<tr>
<td>El Khalidi et al.31</td>
<td>104 patients, 84 w/ AN, 0 AVM</td>
<td>98.8</td>
<td>100</td>
<td>16-detector CT</td>
</tr>
<tr>
<td>Yoon et al.30</td>
<td>85 patients SAH 71 w/ AN, 0 AVM</td>
<td>100</td>
<td>93.3</td>
<td>16-detector, caught 100% of culprit AN</td>
</tr>
<tr>
<td>Agid et al.28</td>
<td>65 patients w/SAH, 47 w/ AN, 0 AVM</td>
<td>97.9 (95% CI = 88.9%–99.9%)</td>
<td>100</td>
<td>64-detector CT</td>
</tr>
</tbody>
</table>

AN = cerebral aneurysm; AVM = arterial venous malformation; CT = computed tomography; CTA = computed tomography angiography; LP = lumbar puncture; SAH = subarachnoid hemorrhage.

For notational purposes we have the following: P(+,+)= the joint probability of a positive criterion standard test for CT and CTA, P1(+|+)= sensitivity of CT (probability of a positive CT, given a true SAH), P2(+|+) = sensitivity of CTA (probability of a positive CTA, given no true SAH), P2(−|+) = specificity of CTA (probability of a negative CTA, given a true aneurysm), P2(−|−) = specificity of CTA (probability of a negative CTA, given no true aneurysm). Note also that P(−|+)= 1 − P(+|+) and that P(|−)= 1 − P(+|−).

Under the independence assumption between the CT and CTA tests, the expected proportion of subjects who are diagnosed as CT+ and CTA+ is given by the product of three probabilities P(+,+)=P1(+|+)P2(+|+). Similarly, the expected proportion of subjects who are diagnosed as CT+ and CTA+ given CT was truly ‘+’ and CTA was truly ‘−’ is given by the product of three probabilities P(+,+)|CT+)=P1(+|+)P2(+|+) and so on as described above. Using the clinical assumptions made (see Table 4) and results from the selected studies, Table 5 illustrates the various test result probabilities.

This model makes a probabilistic argument for CT/CTA in patients with a pretest probability of SAH of 15%. Using the clinical assumptions above and given that the two diagnostic tests are independent, the CI of the posttest probability of both an aneurysm and an SAH being truly present in the face of a two negative results ranges from 0.0% to 0.25%. In other words, there is a posttest probability of 99.98% (95% CI = 99.75% to 100%) that both diseases are not present assuming study independence between CT and CTA.

Test Dependence
This probability model has assumed that CT and CTA are independent tests looking for different diseases (SAH vs. aneurysm). In support of the tests being independent are that the factors that decrease the sensitivity of CT include time from headache onset, hematocrit concentration, and volume of hemorrhage. These factors do not have an adverse effect on the sensitivity of CTA. Factors that would decrease the sensitivity of CTA such as aneurysm size, motion artifact, and intravenous contrast injection technique would not adversely affect
the sensitivity of CT for SAH. However, the independence assumption may not be realistic. These tests are done in immediate sequence using the same technology. The tests are interpreted at the same time by the same examiner, which could threaten their independence.

The most concerning dependent relation is that the same examiner interprets both studies. This may have an additive negative effect if the examiner is not proficient or is distracted. However, the dependence of the two studies may have a positive effect if a subtle finding on one scan causes increased scrutiny when reading the other scan.

Although the dependent effect of the two studies is difficult to determine, the following mathematical construct attempts to assess the effect. Using basic probability relationships, we can drill down into the calculation of the proportion of missed cases assuming some structure with respect to the dependence between CT and CTA in the specific case where both tests are negative when in fact there was an SAH or an aneurysm. This may be carried forth by utilizing the specific calculation of the expected proportion of missed cases, which is now the product of three probabilities $P(+,+)P1(−|+)P2|1((−|+)−(+)−))$, where now $P2|1((−|+)−(+)−))$ corresponds to the conditional probability of the event that CTA was a false negative given that the CT was a false negative. Note that the sensitivity of CTA is “embedded” within $P2|1((−|+)−(+)−))$. To examine the dependence structure, we varied the values of $P2|1((−|+)−(+)−))$ from 0.25 to 0.75, where the level of 0.25 implies a low degree of correlation and the level 0.75 implies a high degree of correlation between the tests with respect to jointly missing a true SAH and a true aneurysm. Although the true dependence is unknown, we have conservatively assumed a 0.5 level of correlation for the purpose of this model based on the previously mentioned factors. This implies that 50% of the time that one study is misread, it will negatively affect the other study’s sensitivity.

Note that the sensitivity for CT scans of 91% (0.91) based on the literature corresponds to $P1(−|+) = 0.09$ in Table 6. Under the independence scenario of the CT and CTA tests in terms of jointly arriving at false negatives, we saw from Table 5 that expected proportion of missed SAH and an aneurysm was calculated to be 0.0002, or 0.02%. From Table 6 we see that between the two tests, the expected proportion of missed SAH and aneurysm with a 25, 50, and 75% study dependence would be 0.0029, 0.0057, and 0.0086, respectively. In other words, assuming a 50% study dependence, the posttest probability would be 99.43% (95% CI = 98.86% to 99.81%) that both diseases are not present.

**DISCUSSION**

If it is acceptable that a small number of SAHs that are not caused by an aneurysm or AVM are missed upon initial evaluation, then the CT/CTA strategy may be an alternative to the current paradigm in select patients. SAH due to perimesencephalic bleeding or in the setting of normal cerebral arteries does not carry the same risk for poor outcome. In patients who are neurologically intact and whose headaches are controlled, discharge should have no ill effect.

If the patient has an aneurysm that has not leaked (i.e., SAH is not present), the current CT/LP strategy is only 96% sensitive. There is still a potential to miss these patients with this CT/CTA strategy. However, CTA has been shown to be very sensitive detecting aneurysms, especially those greater than 3 mm. As the likelihood of rupture is directly related to aneurysm size, missed small aneurysms have a very low risk to subsequently bleed. The excellent outcome on long-term follow-up of patients who underwent CT/LP with negative results shows this to be a safe discharge.

A definitive study would involve a CT/CTA/LP strategy. All patients who had a negative CT/CTA would go on to have LP. This could prove that the CT/CTA strategy is sufficient and that LP offers no additional information. There are some real-world problems with conducting this study. Most importantly, the number of subjects would need to be very large (>3,000 patients). Second, when LP results are inconclusive, CTA is often done as a more definitive study. This research strategy would reverse that logic. Finally, obtaining informed consent is one of the biggest obstacles in obtaining an LP in these patients. Currently, after a negative CT in a patient with a headache of less than 48 hours, the physician can inform the patient that there is approximately a 5%–10% chance of an undetected SAH. When both the CT and the CTA are negative, informed consent should estimate the probability of a missed SAH resulting from an aneurysm or AVM as less than 1%. This could significantly reduce the number of patients who are willing to undergo an LP after negative tests.

In a patient with a pretest probability of less than 15%, a CT/CTA may be a less invasive and more specific diagnostic strategy. As pretest probability decreases, the likelihood of two false-negative tests also decreases. In those cases where LP is technically impos-
sible, or for patients who refuse LP, CT/CTA may offer a reasonable alternative diagnostic strategy.

In those cases with a higher pretest probability due to risk factors, abnormal exam or mental status, or classic presentation, a new diagnostic strategy of CP/CTA/LP may be preferred. The true pretest probability in these patients is unknown, but estimating it to be 25% would increase the posttest probability of two false-negative tests to 0.96% (95% CI = 0.3% to 1.9%), which may be unacceptably high in a high-risk patient.

In those patients with a CT that is negative for SAH, and the CTA shows an aneurysm, an LP will need to be undertaken to distinguish bleeding versus nonbleeding aneurysm. A nonbleeding aneurysm may be followed conservatively after specialty consultation. The true prevalence of incidental aneurysms in acute headache patients who seek care in the ED is unknown. Incidental aneurysm prevalence literature is based on autopsy and angiography studies and varies between 1 and 6%.

More recent angiography studies show a significantly lower percentage (1%–2%) of incidental aneurysms. Rinkel et al. concluded in 1998 that the prevalence of incidental aneurysm in adults without risk factors for SAH is approximately 2%. The only study on ED patients with headache who underwent CTA showed an aneurysm prevalence of 5% (5/106), with 3% (3/106) being culprit lesions, one being potentially symptomatic (1/106), and one being most likely incidental (1/106). The clinical utility of the CT/CTA approach may be determined by the true prevalence of these nonbleeding aneurysms and the implications for patient management and follow-up. Discovering “incidental” aneurysms may subject the patient to additional risk from subsequent testing and interventions.

In the current clinical setting of readily available CT and CTA at most emergency care facilities, this diagnostic strategy may offer an more consistent and less invasive diagnostic work-up of an acute headache. Patients are often reticent to undergo and physicians are hesitant to conduct an LP. Equivocal LP results often cloud the diagnostic picture further. These issues may contribute to suboptimal work-ups and may account for the persistence of an basal rate of “missed bleeds” that was recently demonstrated to be 5% of acute headache patients in Canadian EDs.

LIMITATIONS

This paradigm has some shortfalls, but it attempts to frame the clinical and research questions. It also speaks to current practice that exists at some institutions but has no true supporting literature. Shortfalls of the model include the unknown dependence of the two tests and the true sensitivity of CTA in the absence of SAH in neurologically intact headache patients. However, unlike CT where clinical condition is directly linked to volume of hemorrhage and a worse clinical condition may positively skew CT performance, the same should not be true of CTA.

The level of dependence between the CT and CTA tests is a significant assumption. A test of independence (vs. dependence) between the CT and CTA tests could be carried forth with a small study of roughly 30 to 130 subjects depending upon the specific alternatives via a straightforward test involving Kendall’s tau-b test statistic.

Clinical care shortfalls include the exposure to intravenous contrast and additional radiation, the lack of diagnostic information regarding other conditions obtained from LP (benign intracranial hypertension, meningitis), and an expected increased frequency of detection of nonbleeding “incidental” aneurysms that will require further follow-up.

This is a model and not based on actual study data. A large multicenter study examining acute headache patients who present to the ED with normal neurologic exams who receive CT/CTA and LP should be conducted. These patients should be followed for an extended period of time after discharge as a surrogate to detect missed aneurysms because adding DSA as the criterion standard to CTA would be impractical. Assuming that the current prevalence, sensitivities, and specificities hold true, an equivalence study would require at least 3,000 subjects to be enrolled. The feasibility of such a study is limited. A smaller study could test the dependence assumption in a similar patient population and offer support to this model and practice.

CONCLUSIONS

In ED patients with a complaint of acute-onset headache of less than 48 hours’ duration who have an intact neurologic exam and no significant increased risk of aneurysm, it is reasonable to conclude that computed tomography, followed by computed tomography angiography, has excluded subarachnoid hemorrhage due to aneurysm or arterial venous malformation with a 99% posttest probability. A clinician may choose to spare the lumbar puncture in these cases. At a minimum, informed consent for lumbar puncture should put the theoretical risk of a missed diagnosis of sub-

| CT Sensitivity P₁(+|+) | 1-Sensitivity CT P₂(−|+) | Dependence P₂₁(+|+)P₂+(−|+) | Posttest Probability CT(−|+),CTA(−|+) (95% CI) |
|------------------------|-------------------------|-----------------------------|----------------------------------|
| 91 (82–97)             | 0.09                    | 0.25                        | 0.0029 (0.0057–0.0009)           |
| 91 (82–97)             | 0.09                    | 0.50                        | 0.0057 (0.114–0.0019)            |
| 91 (82–97)             | 0.09                    | 0.75                        | 0.0086 (0.172–0.0029)            |

CT = computed tomography scan; CTA = computed tomography angiogram; SAH = subarachnoid hemorrhage.
arachnoid hemorrhage due to aneurysm or arterial venous malformation after negative computed tomography/computed tomography angiography at less than 1%, assuming a 50% test sensitivity dependence. Patients with classic presentations, meningismus, abnormal neurologic exam, or significant risk factors may warrant computed tomography/lumbar puncture with or without computed tomography angiography.

This model attempts to answer the question of: Can computed tomography/computed tomography angiography replace computed tomography/lumbar puncture in selected patients? The answer is yes. The next question, which will depend on the prevalence of incidental aneurysm, may be: should it?

References


