
From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department with Acute Headache:

Jonathan A. Edlow, MD (Chair)
Peter D. Panagos, MD
Steven A. Godwin, MD
Tamara L. Thomas, MD
Wyatt W. Decker, MD

Members of the American College of Emergency Physicians Clinical Policies Committee (Oversight Committee):

Andy S. Jagoda, MD (Chair 2003-2006, Co-Chair 2006-2007)
Wyatt W. Decker, MD (Co-Chair 2006-2007, Chair 2007-2008)
Deborah B. Diercks, MD
Barry M. Diner, MD (Methodologist)
Jonathan A. Edlow, MD
Francis M. Fesmire, MD
John T. Finnell, II, MD, MSc (Liaison for Emergency Medical Informatics Section 2004-2006)
Steven A. Godwin, MD
Sigrid A. Hahn, MD
John M. Howell, MD
J. Stephen Huff, MD
Eric J. Lavonas, MD
Thomas W. Lukens, MD, PhD
Donna L. Mason, RN, MS, CEN (ENA Representative 2004-2006)
Edward Melnick, MD (EMRA Representative 2007-2008)
Anthony M. Napoli, MD (EMRA Representative 2004-2006)

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ABSTRACT

This clinical policy from the American College of Emergency Physicians is an update of a 2002 clinical policy on the evaluation and management of adult patients presenting to the emergency department (ED) with acute, nontraumatic headache. A writing subcommittee reviewed the literature to derive evidence-based recommendations to help clinicians answer the following 5 critical questions: (1) Does a response to therapy predict the etiology of an acute headache? (2) Which patients with headache require neuroimaging in the ED? (3) Does lumbar puncture need to be routinely performed on ED patients being worked up for nontraumatic subarachnoid hemorrhage whose noncontrast brain computed tomography (CT) scans are interpreted as normal? (4) In which adult patients with a complaint of headache can a lumbar puncture be safely performed without a neuroimaging study? (5) Is there a need for further emergent diagnostic imaging in the patient with sudden-onset, severe headache who has negative findings in both CT and lumbar puncture? Evidence was graded and recommendations were given based on the strength of the available data in the medical literature.

INTRODUCTION

A query of the National Hospital Ambulatory Medical Care Survey for 1999 to 2001 found that headache accounted for 2.1 million emergency department (ED) visits (2.2 % of all ED visits). Of the 14% of the patients who underwent imaging, 5.5% received a pathologic diagnosis. Emergency physicians must determine which patients need neuroimaging in the ED and which can be appropriately deferred and evaluated in the outpatient setting. Many patients have limited access to care, which further complicates this decision process in clinical practice, but this variable is not accounted for in most studies. When evaluating the data, the outcome measures used in determining the need for neuroimaging in the ED must also be clinically relevant to practice. For example, diagnosing a brain tumor may not require immediate neurosurgery or even hospitalization, yet may clearly direct the disposition and follow-up timing of the patient. This policy is an update of the 2002 American College of Emergency Physicians (ACEP) clinical policy on headache.

In deciding which test to perform, emergency physicians must assess pretest risk for the condition. Researchers in Ottawa, Ontario, conducting an observational study in patients with severe headache, asked emergency physicians to rate their comfort level in performing a lumbar puncture without first obtaining a head computed tomography (CT) scan, as well as their estimates of pretest probability of a subarachnoid hemorrhage in these patients. Of the 1,070 eligible patients, 747 were prospectively enrolled, with 50 patients having a confirmed subarachnoid hemorrhage. Emergency physicians were either “uncomfortable” or “very uncomfortable” with performing a lumbar puncture without a head CT scan in 49.6% of 625 patients. They were “very comfortable” with performing a lumbar puncture with a head CT scan in only 10.2% of patients with acute headache. Emergency physicians were better at identifying patients at low risk for subarachnoid hemorrhage and less accurate at identifying the high-risk patients. Emergency physicians’ estimate of the probability of the patient having a subarachnoid hemorrhage revealed a receiver operating characteristic curve with an area of 0.85 (95% confidence interval [CI] 0.80 to 0.91). The sensitivity of clinical suspicion was 93% (95% CI 81% to 97%) and specificity was 49% (95% CI 45% to 53%) using a pretest probability of 2% or greater as the threshold. Researchers believed that emergency physicians discriminate moderately well between headache due to subarachnoid hemorrhage and other causes. However, given the high mortality associated with a missed diagnosis, emergency physicians are currently unwilling to trust their judgment. There were 3 subarachnoid hemorrhage cases in which pretest probability was 2% or lower, which may explain why many emergency physicians continue to use diagnostic tests on patients with low pretest probability.

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. Multiple searches of MEDLINE and the Cochrane database were performed. Specific key word/phrases used in the searches are identified under each critical question. To update the 2002 ACEP policy, which used literature up to December 1999, all searches were limited to English-language sources, human studies, adults, and years January 2000 to August 2006. Additional articles were reviewed from the bibliography of articles cited and from published textbooks and review articles. Subcommittee members supplied articles from their own files, and more recent articles identified during the expert review process were also included.

The reasons for developing clinical policies in emergency medicine and the approaches used in their development have been enumerated. This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the existing literature; when literature was not available, consensus of emergency physicians was used. Expert review comments were received from individual emergency physicians and from individual members of the American Headache Society and the Society for Academic Medicine. Their responses were used to further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy. This document was also reviewed by the Joint Guidelines Committee (JGC) of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), however, this review does not constitute an endorsement or approval of the document, its content, or conclusions by the JGC, the AANS, or the CNS. Clinical policies are scheduled for revision every 3 years.
However, interim reviews are conducted when technology or the practice environment changes significantly.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic clinical reports, respectively (Appendix A). Articles were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (eg, selection, detection, transfer), external validity (ie, generalizability), and sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula, taking into account design and quality of study (Appendix B). Articles with fatal flaws were given an “X” grade and not used in formulating recommendations in this policy. Evidence grading was done with respect to the specific data being extracted and the specific critical question being reviewed. Thus, the level of evidence for any one study may vary according to the question, and it is possible for a single article to receive different levels of grading as different critical questions are answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of this policy.

Clinical findings and strength of recommendations regarding patient management were then made according to the following criteria:

**Level A recommendations.** Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

**Level B recommendations.** Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

**Level C recommendations.** Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

This policy is not intended to be a complete manual on the evaluation and management of adult patients with acute headache but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain enough quality information to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. ACEP clearly recognizes the importance of the individual physician’s judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the crucial questions addressed in this policy.

**Scope of Application.** This guideline is intended for physicians working in hospital-based EDs.

**Inclusion Criteria.** This guideline is intended for adult patients presenting to the ED with acute, nontraumatic headache.

**Exclusion Criteria.** This guideline is not intended to address the care of pediatric patients or the care of patients with trauma-related headaches.

**CRITICAL QUESTIONS**

1. Does a response to therapy predict the etiology of an acute headache?

**Patient Management Recommendations**

**Level A recommendations.** None specified.

**Level B recommendations.** Pain response to therapy should not be used as the sole diagnostic indicator of the underlying etiology of an acute headache.

Key words/phrases for literature searches: thunderclap headache, acute headache, response to therapy, cause or etiology, and variations and combinations of the key words/phrases.

Because headache is a common complaint, physicians have sought ways to differentiate the serious life-, limb-, vision-, or brain-threatening etiologies from the more benign ones. Defining who can be sent home safely without workup beyond medical history and physical examination could expedite patient care while decreasing patient cost. Anecdotally, some clinicians have tried to use a favorable response to medications as an indicator that a patient’s headache is not due to a secondary (serious) etiology. To fully address this question, it is important to understand the underlying pathophysiology of headache and the pharmacologic rationale behind the current concepts in therapy.

Current understanding of headache suggests that there is a common pathway for the pain regardless of the underlying etiology. Much of our understanding about the pathophysiologic characteristics comes from research on migraine. In essence,
headache can be caused by (1) distention, traction, or dilation of intracranial or extracranial arteries; (2) traction or displacement of large intracranial veins or the dural envelope; (3) compression, traction, or inflammation of cranial and spinal nerves; (4) head and neck muscle spasm, inflammation, or trauma; (5) meningeal irritation; (6) raised intracranial pressure; and (7) disturbance of intracerebral serotonergic projections.

Evidence suggests that headache pain is transmitted by the trigeminal nerve from the blood vessels of the pia mater and dura mater. The exact trigger of the pain may be multifactorial, but once the trigger occurs, the trigeminovascular axons are stimulated, resulting in the onset of pain and release of neurogenic peptides stored in the afferent C fibers innervating cephalic blood vessels. These vasoactive neuropeptides then stimulate endothelial cells, mast cells, and platelets, creating an inflammatory cascade known as “neurogenic inflammation.” Vasodilatation with enhanced permeability of plasma proteins follows with a perivascular inflammatory reaction. “Neurogenic inflammation” within the cephalic tissue is one model that has been proposed as the pathogenic mechanism of headache. However, selective and potent inhibitors of “neurogenic inflammation” have thus far proven ineffective in clinical trials.

Serotonin (5-HT) receptors are the main focus of pain management because they are known to modulate neurogenic peptide release and vasoconstrict dilated dural vessels. The goal of therapy is to prevent or abort the neurogenic inflammation that occurs as a result of neuropeptide release. Subtypes of the 5-HT1 receptor are believed to be the most important receptors in the final common pathway of headache. Despite many adverse effects, 5-HT is a potent vasoconstrctor, a property that may be a factor in its ability to treat migraines. Pharmacologic agents with an affinity for 5-HT receptors are currently the preferred therapy in acute headache management. Some agents, such as the triptans, are specific agonists at the 5-HT1 receptor, whereas other medications, such as dihydroergotamine, prochlorperazine, and metoclopramide, act at a variety of 5-HT and other aminergic receptors.

There are no prospective randomized controlled trials, evidence from meta-analysis from randomized controlled trials, or well-designed cohort studies to support or refute the practice of using response to therapy in nontraumatic headaches as an indicator of potential underlying pathologic entities. The only published data about response to pain medications as an indicator of underlying headache etiology is in Class III evidence in the form of case reports and case series.

Numerous articles have described headaches of varying secondary (serious) etiologies showing clinical improvement or resolution of pain in response to many different analgesics. These conditions include but are not limited to the following: intracerebral hemorrhage/subarachnoid hemorrhage (ibuprofen, ketorolac, prochlorperazine), viral meningitis/meningeal carcinomatosis (dihydroergotamine and metoclopramide), carbon monoxide–induced headache (sumatriptan), cerebral venous thrombosis (sumatriptan and various common analgesics), carotid artery dissection (sumatriptan), subarachnoid hemorrhage (sumatriptan), and cysts of the cava septi pellucidi (indomethacin).

2. Which patients with headache require neuroimaging in the ED?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations.

1. Patients presenting to the ED with headache and new abnormal findings in a neurologic examination (eg, focal deficit, altered mental status, altered cognitive function) should undergo emergent* noncontrast head CT.

2. Patients presenting with new sudden-onset severe headache should undergo an emergent* head CT.

3. HIV-positive patients with a new type of headache should be considered for an emergent* neuroimaging study.

Level C recommendations. Patients who are older than 50 years and presenting with new type of headache but with a normal neurologic examination should be considered for an urgent† neuroimaging study.

*Emergent studies are those essential for a timely decision regarding potentially life-threatening or severely disabling entities. †Urgent studies are those that are arranged prior to discharge from the ED (scan appointment is included in the disposition) or performed prior to disposition when follow-up cannot be assured. Routine studies are indicated when the study is not considered necessary to make a disposition in the ED.

Key words/phrases for literature searches: acute headache, diagnostic imaging, CT scan, MRI, emergency department, and variations and combinations of the key words/phrases.

The primary focus in obtaining a neuroimaging study in the ED is to identify a treatable lesion. Treatable lesions include tumors, vascular malformations, aneurysms, subarachnoid hemorrhage, cerebral venous sinus thrombosis, subdural and epidural hematomas, infections, stroke, hydrocephalus, and others. These positive findings may provide tangible outcomes that can be clearly assessed from a clinical and financial perspective. Less tangible is the impact of reassurance to the patient who has a normal study result. In one study, 60% of patients presenting with headache to an outpatient neurology clinic had concerns of harboring significant pathologic findings, and 40% of those reassured that they had no reason for concern left questioning their evaluation.

The need for neuroimaging in headache patients has been addressed in 5 previous guidelines. Although some of their recommendations are relevant to the acute setting, 3 of them focus more on patients with chronic headache in the primary care setting. In addition to noncontrast head CT scan, contrast
brain CT, CT angiography, and magnetic resonance imaging (MRI) may also be useful, depending on the differential diagnosis and other characteristics of the individual patient.

The cornerstone to assessing the patient with a headache is the medical history and physical examination. Although this seems obvious, it is worth emphasizing because no decisionmaking can take place without appropriate data. There exists significant variation in the literature as to what are important historical and clinical markers. There is also considerable contradiction in the literature about the positive predictive value of specific findings. An abnormal finding on neurologic examination is frequently cited as an indication for emergent neuroimaging. In a Class II study, Ramirez-Lassepas et al reviewed the records of 468 patients who presented to the ED with a chief complaint of headache. The authors reported that abnormal findings in a neurologic examination had a positive predictive value of 39% for intracranial pathology. The US Headache Consortium, in their review of articles dealing with chronic headache, calculated likelihood ratios (LRs) for patients presenting with headache and focal neurologic findings. They reported that the presence of an abnormality on the neurologic examination increased the likelihood of positive results 3-fold (95% CI 2.3 to 4.0) in a neuroimaging study. Normal findings in a neurologic examination reduced the odds of positive findings in a neuroimaging study by 30%.

Historical findings that have prompted neuroimaging in headache patients include older age. These various studies used different age cut-offs in the range of 50 years to 60 years, and it is important to recognize that age is not a dichotomous variable. Adding to this literature, a multivariate analysis of the results from the 1999 to 2001 National Hospital Ambulatory Medical Care Survey for headache on all available historical factors revealed that patients over 50 years of age were more likely to receive a pathologic diagnosis (odds ratio [OR] 3.3, CI 1.2 to 9.3). No additional risk factors were identified from this latter study. Other historical findings for initiation of neuroimaging include occipital location of pain, worsening of headache with Valsalva, headache waking patient from sleep, and headache associated with syncope, nausea, or sensory distortion. The Headache Consortium calculated likelihood ratios for each of these symptoms and, based on the best available evidence in the literature, found that these symptoms may increase the probability of positive findings in a neuroimaging study but reported that the CIs are so wide that clear recommendations could not be made.

Three subsets of headache patients deserve special mention: those presenting with acute sudden-onset severe headache, HIV-positive patients presenting with a new or different headache, and pregnant patients. Acute sudden-onset, severe headache (sometimes referred to in the literature as thunderclap headache) prompts concerns for subarachnoid hemorrhage or other serious intracranial pathology. The term thunderclap headache, first used by Day and Raskin, describes a sudden-onset headache whose intensity is severe (usually described as worst of life, or excruciating) and reaches that maximal intensity within seconds to a minute. There are many causes of thunderclap headache, many of them serious. The term “sudden-onset severe headache” will be used synonymously with thunderclap headache in the remainder of this document.

Although most patients with sudden-onset severe headache have benign causes, the best data suggest that between 10% and 15% have more serious pathology, most commonly subarachnoid hemorrhage. Mitchell et al reported on 27 patients with the “worst headache of their life,” and only 1 had intracranial pathology. Ramirez-Lassepas et al reviewed 468 headache patient records and found no association between the patient’s description of the headache and the final diagnosis. Reinus et al retrospectively studied 333 patients with an acute headache; 17 presented with the “worst headache of their life” complaint, yet only 1 had positive findings when a head CT was performed ( lumber puncture results were not reported). Conversely, Harling et al prospectively studied patients presenting with a thunderclap headache; of 49 patients, 35 had a subarachnoid hemorrhage. Lledo et al prospectively studied all patients presenting during a 1-year period with severe sudden-onset headache. Of 27 patients enrolled, 9 had subarachnoid hemorrhage, 1 had intraventricular hemorrhage, and 2 had meningitis. Only 4 of the 9 patients had positive CT results, but patients in this study were late presenters (mean delay 72 hours after onset of headache for the subarachnoid hemorrhage patients). In a prospective study, Mills et al reported that 29% of patients complaining of the “worst headache of their life” had positive findings on head CT scan. The case of a patient with a thunderclap headache, it is still recommended that the patient undergo emergent neuroimaging followed by a cerebrospinal fluid (CSF) analysis. This topic is more thoroughly discussed in Question 3.

In the United States, the overall decreased incidence of HIV seroconversion combined with improved antiviral therapy has decreased the number of acutely ill HIV patients seen in the ED. Yet, as the disease advances, patients with HIV disease frequently have central nervous system processes that include space-occupying lesions. Lipton et al reported on 49 HIV patients presenting with a chief complaint of headache, 35% of whom were found to have a mass lesion. Rothman et al prospectively studied 110 HIV patients with neurologic complaints, searching for predictors of new focal central nervous system lesions. Twenty-four percent of the patients were found to have a focal lesion. Using multivariate logistic regression analysis, new seizure, depressed or altered orientation, and headache that was different in character from previous ones or that lasted more than 3 days predicted a focal brain lesion. The presence of 1 or more of these 4 clinical findings identified all patients with focal lesions; these data have not been prospectively validated. As reported in other headache studies, focal motor deficit had a strong
During pregnancy and the puerperium, it has been reported that the incidence of stroke increases 3- to 13-fold. Headache is frequently the symptom that prompts an emergent evaluation in these patients. The majority of pregnant women with headaches have benign causes. In one non-ED series of more than 1,100 pregnant women with headache, a very small number had serious secondary causes. Although no reliable data exist, subarachnoid hemorrhage is thought to be increased during pregnancy, delivery and the puerperium, occurring in roughly 20 per 100,000 deliveries. Case reports illustrate other serious causes of headache such as carotid dissections, venous sinus thrombosis, and ruptured arteriovenous malformation. Although these data illustrate the increased risk of adverse events in pregnant patients with headache who may present to the ED, there are insufficient data to drive any firm recommendations in this group of patients.

3. Does lumbar puncture need to be routinely performed on ED patients being worked up for nontraumatic subarachnoid hemorrhage whose noncontrast brain CT scans are interpreted as normal?

**Patient Management Recommendations**

**Level A recommendations.** None specified.

**Level B recommendations.** In patients presenting to the ED with sudden-onset, severe headache and a negative noncontrast head CT scan result, lumbar puncture should be performed to rule out subarachnoid hemorrhage.

**Level C recommendations.** None specified.

Key words/phrases for literature searches: subarachnoid hemorrhage, acute imaging, lumbar puncture, and variations and combinations of the key words/phrases.

The presenting symptom for subarachnoid hemorrhage for most patients presenting to the ED is a sudden, severe-onset headache unlike any previous episode. The most common etiology of nontraumatic subarachnoid hemorrhage is the rupture of an aneurysm in the Circle of Willis. Because early, accurate detection of subarachnoid hemorrhage has been shown to improve outcomes, it is imperative that the clinician attempt to accurately identify these patients to prevent further morbidity and mortality.

After a focused medical history and physical examination for the patient with a sudden-onset, severe headache, most patients undergo noncontrast CT imaging to rule out a subarachnoid hemorrhage. Noncontrast CT scanning in patients presenting to the ED for an acute headache has become increasingly easier to access. After a normal head CT scan result, patients with initially low pretest probability for subarachnoid hemorrhage may undergo additional testing, such as the lumbar puncture and CSF analysis. The lumbar puncture is considered the criterion standard for diagnosing subarachnoid hemorrhage because it may detect small amounts of xanthochromia or blood in the CSF that can be missed by CT.

Xanthochromia, which is the yellow color caused by bilirubin and oxyhemoglobin due to lysis of erythrocytes, can be detected by either visual inspection or spectrophotometry. Because bilirubin formation is an enzyme-dependent, invivo process, xanthochromia takes hours after the bleed to occur. Spectrophotometry is more sensitive, but this greater sensitivity comes at the expense of low-to-moderate specificity. Furthermore, data suggests that clinicians using visual inspection identify those samples that contained significant amounts of bilirubin. Finally, spectrophotometry is not available in the majority of North American hospital clinical laboratories. Visual inspection of CSF for xanthochromia still requires proper technique. The CSF must be rapidly centrifuged, and the supernatant should be carefully compared to an identical tube filled with an equal volume of tap water against a white background.

However, the lumbar puncture is an invasive procedure associated with patient discomfort because of needle insertion, local tissue irritation, and reflex muscle spasm, as well as complications such as postdural puncture headache, nerve injury, epidural hematoma, and meningitis. Furthermore, false-positive results lead to more invasive testing. Morgenstern et al found that emergency physicians omitted doing a lumbar puncture in patients for the workup of their "worst headache of life" in 50% of cases.

Clinicians must understand the limitations of brain CT scanning. Limitations include (1) the technical inability of scanners to identify small hemorrhages in areas obscured by artifact or bone; (2) the inability to diagnose idiopathic intracranial hypertension, meningitis, or carotid or vertebral artery dissection, some cases of cerebral venous sinus thrombosis and pituitary apoplexy, and spontaneous intracranial hypotension; (3) the varied levels of expertise of the reader; (4) spectrum bias in small-volume subarachnoid hemorrhage; (5) decreased sensitivity for blood in the setting of anemia; and (6) decay in sensitivity with time.

As for spectrum bias, the sensitivity of CT is decreased for detecting subarachnoid hemorrhage in patients with "minor leaks" and those with normal neurologic examination results. The sensitivity also decreases with time from onset of headache. This is because of the dilution and degradation of blood that occurs as CSF flows through the subarachnoid space. The International Cooperative Study on the Timing of Aneurysm Surgery evaluated 3,500 patients with aneurysmal subarachnoid hemorrhage with early 1980 CT scanners and found a decrease in positive scan results from 92% on the day of rupture to 86% at 1 day later, 76% at 2 days, and 58% 5 days later. Several additional studies using modern CT scanners have shown a consistent decrease in sensitivity in detecting blood as time elapses from symptom onset. Last, as the hematocrit level decreases, blood will appear isodense with brain tissue and can be easily overlooked by the reviewer; this occurs at hemoglobin concentrations below 10 g/dL.

Recent advances in CT technology have improved the accuracy of CT scans compared with third-generation scanners.
from the 1980s and 1990s. Previous sensitivities in these scanners for detecting subarachnoid hemorrhage have been from 92% to 98%, 38,60,61

The lumbar puncture also has well-defined limitations in diagnosing subarachnoid hemorrhage and other significant intracranial pathologic entities. These include unruptured aneurysm, arterial dissection or cerebral venous sinus thrombosis, and pituitary apoplexy, all of which can present in a manner similar to subarachnoid hemorrhage and which may not be identified if only a lumbar puncture is performed. The lumbar puncture may be time consuming and can be technically difficult in uncooperative or obese patients. Contamination of the CSF with venous blood introduced during the procedure may make interpretation of CSF difficult. The Class III study by Shah et al. 63 found the incidence of traumatic lumbar puncture in the ED was 13.3%, using 400 RBCs as the cutoff and 8.9% using 1,000 RBCs as the cutoff with higher percentages when the lumbar puncture was done on the inpatient service. Finally, there is morbidity, including the risk of postdural puncture headache. 64 Additional potential information from the lumbar puncture that often goes unused is an initial opening pressure. Measuring the opening pressure can be helpful in distinguishing a traumatic puncture from a true subarachnoid hemorrhage (in which two thirds of cases show an elevated pressure), as well as for providing additional information for other diagnoses such as spontaneous intracranial hypotension, benign intracranial hypertension, and cerebral venous sinus thrombosis, all of which can present with severe headache. 50,65-67

Several studies have attempted to quantify the value of CT scanning and lumbar puncture in patients with suspected subarachnoid hemorrhage. Previous estimates have found rates of subarachnoid hemorrhage confirmed by lumbar puncture (after normal CT scan results) of 2.5% to 3.5%. 58 In a Class II study of 592 patients presenting to the ED with acute, severe headache, 61 had subarachnoid hemorrhage; of these, 55 were diagnosed by CT and 6 by lumbar puncture. 68 Foot and Staal 69 performed a retrospective chart review (Class III) of 196 patients who had CSF analysis to risk stratify for subarachnoid hemorrhage. All 6 patients underwent angiotherapy; 4 results were normal and 2 showed aneurysms.

Advanced imaging techniques are increasingly available that may facilitate more accurate and timely diagnosis of disease in the acute headache patient. Boesinger and Shiber 71 performed a Class III retrospective chart review of ED headache patients during a 1-year period who had both a CT scan (fifth generation, multislice detector) and lumbar puncture. Of the 177 patients who were analyzed, no patient with a negative CT scan result had a subarachnoid hemorrhage. However, a more recent Class III study of 149 patients with subarachnoid hemorrhage, which also used a multislice scanner, found a sensitivity for CT of 93% for all patients and a sensitivity of 90% for those less affected patients presenting with headache and a normal mental status. 62 The totality of the evidence suggests that lumbar puncture must still be performed after a negative CT scan result in patients being evaluated for subarachnoid hemorrhage.

Despite the relatively rapid advancement of imaging technology available to the emergency physician, the diagnosis of severe headache is challenging and often requires a high degree of suspicion and clinical acumen. To date, no single noninvasive imaging modality is 100% sensitive in detecting acute subarachnoid hemorrhage and the other significant intracranial lesions responsible for the severe headache presentation. In the future, additional studies will need to focus on the decisionmaking process, accurate risk stratification, pre- and posttest disease probability and Bayesian analysis, allowing for the proper use of technology to aid in the decision process to rule out subarachnoid hemorrhage in the severe headache patient.

4. In which adult patients with a complaint of headache can a lumbar puncture be safely performed without a neuroimaging study?

**Patient Management Recommendations**

**Level A recommendations.** None specified.

**Level B recommendations.** None specified.

**Level C recommendations.**

1. Adult patients with headache and exhibiting signs of increased intracranial pressure (eg, papilledema, absent venous pulsations on funduscopic examination, altered mental status, focal neurologic deficits, signs of meningeal irritation) should undergo a neuroimaging study before having a lumbar puncture.

2. In the absence of clinical findings suggestive of increased intracranial pressure, a lumbar puncture can be performed without obtaining a neuroimaging study. **(Note: A lumbar puncture does not assess for all causes of a sudden severe headache.)**

Key words/phrases for literature searches: acute headache, lumbar puncture, subarachnoid hemorrhage, neuroimaging, head CT, diagnostic imaging, and variations and combinations of the key words/phrases.

In patients with acute headache, head CT and CSF analysis are used alone and in combination to diagnose life-threatening entities, including mass lesions, intracranial hemorrhage, and infection. There are times when CSF analysis alone would suffice; however, concern of causing herniation because of increased intracranial pressure often prompts obtaining a head
CT scan before a lumbar puncture. To choose the appropriate diagnostic study, it is important to know the indications and limitations of the study. If a CSF analysis is the only test needed, it is important to recognize which patients can have a lumbar puncture safely performed without risk of herniation.

The risk of herniation has been the paramount concern of clinicians who perform lumbar punctures. The earliest description of this complication was reported 6 years after Heinrich Quincke performed the first lumbar puncture in 1890. Four deaths resulting from herniation were reported by Furbinger in 1896; the increased intracranial pressure was attributed to cerebellar neoplasms in 2 cases, to a cerebellar abscess in 1 case, and to a frontal tumor in 1 case. Although herniation is a rare occurrence overall, other case reports have been published since these earliest observations describing cerebral herniation resulting from the performance of a lumbar puncture. Interestingly, one study of a small number of patients with intracranial pressure monitors in place suggested that intracranial pressure could be estimated by measurement of intraocular pressure.

There are no prospective, controlled trials testing the safety of performing a lumbar puncture before a neuroimaging study in patients with a chief complaint of headache. One study addressed this question using a mathematical model in which lumbar puncture would be the first diagnostic test for the acute-onset headache patient with suspected subarachnoid hemorrhage and found that for every 100 patients, the “lumbar puncture first” model would result in significantly fewer CT scans (79 to 83) and a few additional lumbar punctures (7 to 11). This hypothesis has never been tested in a clinical trial. For ethical reasons, it is unlikely that patients with focal neurologic findings, altered mental status, or other evidence of increased intracranial pressure will ever be enrolled as subjects in a controlled trial in which a lumbar puncture is performed before a neuroimaging study.

Two case series by Duffy describe occurrences of herniation in patients with known or strongly suspected intracranial hematomas. In one report, 10 of 30 patients stopped breathing or developed unequal pupils while the lumbar puncture needle was still in place or shortly after it was removed. Fifteen of the 30 patients had marked deterioration within 24 hours of the procedure. The relative contributions of the lumbar puncture versus the natural disease course to the patients’ clinical deterioration is not known. All 30 patients in this report had significant clinical findings such as a focal neurologic examination, progressive mental status changes, papilledema, “meningitic symptoms,” or abnormal cranial radiographs. In another case series, 44 of 74 patients underwent lumbar puncture before neuroimaging. All of the patients were drowsy, confused, or had neurologic deficits. Seven had clinical deterioration at the time of lumbar puncture, and all of these had an intracranial hematoma.

A case series reported from Australia in 1985 described lumbar puncture in 70 patients who had a “mild hemiparesis,” had drowsiness, or were confused. Only 1 of the 70 patients, a patient with a subarachnoid hemorrhage, deteriorated after the lumbar puncture and died 12 days later.

Whereas Duffy’s case series suggest the high likelihood of an adverse outcome if a patient with a space-occupying lesion undergoes a lumbar puncture, a 1988 Class III report by Zisfein and Tuchman had the opposite finding. Thirty-eight patients with head CTs demonstrating an intracranial mass underwent lumbar puncture “to rule out meningitis.” All patients had an abnormal mental status or focal neurologic examination before undergoing the procedure. Thirty-four patients (89%) had evidence of a mass effect on head CT. The central nervous system pathologic processes included hematomas, abscesses, and dural collections. No significant neurologic deterioration was noted in 37 of 38 patients. One patient who had no brainstem function (absent caloric reflexes, dilated and fixed pupils) before the lumbar puncture died after the procedure.

Patients with a headache, a normal neurologic examination, a normal mental status, a normal funduscopic examination, and no meningeal signs are theoretically the best candidates for the “lumbar puncture without CT” strategy. To characterize patients who could safely undergo a lumbar puncture without prior neuroimaging, researchers at Duke University Medical Center, in a Class II study, asked internal medicine residents supervised by ED attendings to complete standard forms before CT scan of all patients who presented to the ED and needed an emergent lumbar puncture. The reasons for emergent lumbar puncture were suspected meningoitis (37%), suspected subarachnoid hemorrhage (42%), and other (21%). The physicians recorded their impression of the likelihood that a patient would have a CT finding that contraindicated dural puncture. Seventeen of 111 enrolled patients had a new central nervous system abnormality. Three of these 17 had contraindications to spinal tap (as defined by CT findings). Clinical findings that predicted abnormal CT results with statistical significance were altered mental status (positive LR 2.2; 95% CI 1.5 to 3.2), papilledema (+LR 11.1; 95% CI 1.1 to 115), and focal neurologic findings (+LR 4.3; 95% CI 1.9 to 10). The physician’s clinical impression had the highest predictive value in identifying patients with a contraindication to lumbar puncture (+LR 18.8; 95% CI 4.8 to 43). Physicians identified the 3 patients with contraindications to lumbar puncture. Clinical attributes, including the diagnosis of HIV disease or having HIV risk factors, history of a central nervous system mass lesion, or a history of malignant neoplasm, were not statistically significant in predicting patients in whom a lumbar puncture was contraindicated, a finding that could be a consequence of the study’s small sample size. The study did not specifically address patients suspected of having subarachnoid hemorrhage, nor did it provide outcome data using a “lumbar puncture first” strategy; therefore, a uniformly favorable result cannot be assumed without prospective validation studies.
5. Is there a need for further emergent diagnostic imaging in the patient with sudden-onset, severe headache who has negative findings in both CT and lumbar puncture? Patient Management Recommendations

**Level A recommendations.** None specified.

**Level B recommendations.** Patients with a sudden-onset, severe headache who have negative findings on a head CT, normal opening pressure, and negative findings in CSF analysis do not need emergent angiography and can be discharged from the ED with follow-up recommended.

**Level C recommendations.** None specified.

Key words/phrases for literature searches: headache, thunderclap headache, emergency angiography, cerebrovascular disorders, glaucoma (acute angle closure), meningitis, brain neoplasm, temporal arteritis, pseudotumore cerebri, hypertensive encephalopathy, carbon monoxide poisoning, medical errors, and variations and combinations of the key words/phrases.

Because patients with sudden-onset, severe headache due to subarachnoid hemorrhage and those due to benign causes cannot be distinguished clinically, all patients with sudden-onset, severe headache require a workup for subarachnoid hemorrhage (noncontrast CT scan and a lumbar puncture looking for blood or xanthochromia if the CT result is normal or nondiagnostic). It is important to emphasize that there is a differential diagnosis to sudden-onset, severe headache beyond simply subarachnoid hemorrhage and benign causes and therefore, in patients whose presentations suggest other causes such as pituitary apoplexy, cerebral venous sinus thrombosis, arterial dissections, and cerebellar stroke, further diagnostic testing may be indicated.

The current teaching is that if both tests yield negative results, subarachnoid hemorrhage is ruled out. The timing of the lumbar puncture may be critical in this decisionmaking process. It has been suggested that lumbar punctures performed prior to 12 hours from onset of symptoms may give false-negative results either because blood has not diffused down or because sufficient time has not elapsed to allow for xanthochromia to appear. Older data collected from the pre-CT era, when lumbar puncture was the primary method to diagnose subarachnoid hemorrhage, show that even in those patients undergoing lumbar puncture in the first 12 hours after headache onset, all had RBCs in the lumbar theca. Also, 60% (43 of 72 lumbar punctures performed prior to 12 hours from onset of headache; show that even in those patients undergoing lumbar puncture in the first 12 hours after headache onset, severe headache patient with an initially normal evaluation. Because neither CT nor MRI can exclude subarachnoid hemorrhage with 100% reliability, CT and lumbar puncture is still considered the standard method to evaluate these patients. Although it is clear that noninvasive imaging, including angiography, will sometimes diagnose the other medical conditions mentioned above, they will also diagnose incidental aneurysms in 2% to 6% of the general population that are not causing the patient’s symptoms and which will result in more unnecessary diagnostic and therapeutic procedures.

A primary concern of most clinicians is the short-term outcome of the acute headache patient presenting to the ED. The most effective evaluation is one that identifies all acute illness and any underlying lesions that place these patients at further risk for an adverse outcome. In the setting of sudden-onset, severe headache, no subarachnoid hemorrhage or sudden death during a 1-year follow-up has been used as a proxy outcome measure.

The largest study addressing this issue is by Perry et al, who published a Class II study of 592 patients with acute severe headache presenting to 2 Canadian EDs and who had a CT and lumbar puncture; 61 (10.3%) had subarachnoid hemorrhage. They followed the patients with negative CT and lumbar puncture results for 6 to 36 months; none was found to have a subsequent subarachnoid hemorrhage, although a single patient was later found to have an unruptured aneurysm that the treating neurosurgeon did not think was related to the earlier headache.

Two other, smaller Class II studies have shown similar results in patients followed up at 1 year. In 2002, Landtblom et al published a Class II prospective cohort study on 137 consecutive patients with sudden-onset, severe headache and presenting to the ED in Sweden. The study was accomplished in 2 phases. During the second phase of their study, which was designed to measure the frequency of subarachnoid hemorrhage, 9 of 80 (11%) patients had subarachnoid hemorrhage. Patients whose workup for subarachnoid hemorrhage (CT and lumbar puncture) was negative were followed for 1 year; none went on to have a subsequent subarachnoid hemorrhage. They concluded that angiography is not routinely necessary in this group of patients.

In 1994, a Class II study by Linn et al reported on 148 patients with acute severe headache. Of this group, 103 patients had acute severe headache and no other neurologic findings. Of the 103, 12 (12%) had subarachnoid hemorrhage and 4 had other neurologic diagnoses established in their workups. Of the patients for whom no diagnosis was made by CT and lumbar
puncture, none was found to have subarachnoid hemorrhage or sudden death during 1 year of follow-up.

Wijdicks et al\(^{36}\) conducted a Class III retrospective follow-up study during a 3.3-year period on 71 patients, each of whom presented with a thunderclap headache with negative findings for subarachnoid hemorrhage in both a CT scan and lumbar puncture. Angiograms were performed on 6 of 71 patients; all results were negative. None of 71 patients had subarachnoid hemorrhage during the 3.3-year follow-up period.

Furthermore, Harling et al\(^{25}\) performed a small, Class III, prospective study on 49 patients with thunderclap headache. Fourteen of 49 patients presenting with thunderclap headaches had negative findings on both a CT scan and lumbar puncture. These patients were followed for a minimum of 18 months, and none had subarachnoid hemorrhage.

The previous studies must be balanced by several case reports and case series that indicate that some patients with unruptured aneurysms (but not subarachnoid hemorrhage) can present with acute severe headache.\(^{33,84-87}\) In the first of these reports,\(^{33}\) an angiogram showed cerebral vasospasm and an unruptured aneurysm. Because patients with “benign thunderclap headache” angiogram showed cerebral vasospasm and an unruptured aneurysm. Because patients with “benign thunderclap headache” aneurysms,\(^{88,89}\) the aneurysm in this case may have been an incidental finding. Taken together, these 5 studies suggest that in some patients with severe, sudden-onset headaches, cerebral vasospasm is a clue to the presence of an aneurysm,\(^{88,89}\) the aneurysm in this case may have been an incidental finding. Taken together, these 5 studies suggest that in some patients with severe, sudden-onset headaches, cerebral vasospasm is a clue to the presence of an aneurysm.

With the increased availability of advanced CT multimodal imaging in the ED, emergency physicians have an enhanced ability to obtain information in properly selected patients. Carstairs et al\(^{90}\) conducted a Class II study assessing the ability of CT angiography, along with CT and lumbar puncture, to diagnose subarachnoid hemorrhage in ED patients presenting with headache. This study used CT angiography, in addition to standard CT and lumbar puncture, to assist in the diagnosis of subarachnoid hemorrhage. Of 106 patients completing the study (of the 116 enrolled), 6 were found to have aneurysms by CT angiography, which is close to the prevalence that would be expected from autopsy figures.\(^{91}\) Of those 6, 3 had either a positive CT or lumbar puncture result. Of the remaining 3, 1 was found to have a false-positive CT angiography result and 1 patient declined surgery and remained asymptomatic, suggesting she had an incidental aneurysm. This study has several limitations, the most important of which is the unproven assumption that the simultaneous presence of an aneurysm and a headache equates with subarachnoid hemorrhage. The strategy of using advanced imaging techniques in the ED evaluation of headache is unproven but merits additional study.

**Relevant industry relationships of subcommittee members:** There were no relevant industry relationships disclosed by the subcommittee members.

**REFERENCES**


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<tr>
<td>Goldstein et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2006</td>
<td>Retrospective case cohort of all US ED headaches</td>
<td>Database query of ED headaches and characteristic of these visits</td>
<td>Testing utilization; demographic trends</td>
<td>Variation in imaging use; age relation to pathology</td>
<td>Follow-up limited; data from ED records</td>
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<tr>
<td>Perry et al&lt;sup&gt;2&lt;/sup&gt;</td>
<td>2005</td>
<td>Prospective cohort during 2 ½ y period; consecutive patients &gt;15 y of age with a nontraumatic acute headache (onset to peak headache less than 1 h) and normal neurologic examination</td>
<td>Attitudes and judgment of emergency physicians in management of acute headache</td>
<td>Pretest ability of physicians to predict subarachnoid hemorrhage</td>
<td>747 patients enrolled; emergency physicians reported being “uncomfortable” or “very uncomfortable” with performing LP without CT in 49.6% of cases and in 75.4% of cases they were uncomfortable in performing no tests; in only 10.2% of the cases, emergency physicians were “very comfortable” with performing an LP without CT; although emergency physicians were able to discriminate subarachnoid hemorrhage from causes of headache, they were generally not willing to perform an LP without first obtaining a head CT scan</td>
<td>Inclusion criteria allowed less severe headaches to be enrolled by including headaches with slower onset (up to 1 h); although prospective data were completed for historical and physical findings for 747 patients, responses were missing for comfort and predictive questions making only 625 patients for LP question, 659 for no testing, and 639 for pretest probability; lack of standard definition of a positive subarachnoid hemorrhage</td>
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<td>Seymour et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>1995</td>
<td>Case series</td>
<td>3 cases of patients with intracranial hemorrhage presenting with headache who responded to analgesics</td>
<td>Pain relief/none</td>
<td>These 3 patients had significant relief with ketorolac or prochlorperazine</td>
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<tr>
<td>Gross et al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>1995</td>
<td>Case series</td>
<td>3 cases of headache patients with inflammatory processes (infectious or carcinomatous meningitis) who responded to analgesics</td>
<td>Pain relief/none</td>
<td>These 3 patients had significant relief with dihydroergotamine or metoclopramide</td>
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<tr>
<td>Lipton et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>1997</td>
<td>Case report</td>
<td>1 patient with carbon monoxide poisoning who received sumatriptan</td>
<td>Pain relief/none</td>
<td>Single patient with carbon monoxide poisoning had pain relief with sumatriptan</td>
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<tr>
<td>Agostoni&lt;sup&gt;13&lt;/sup&gt;</td>
<td>2004</td>
<td>2 case series, 1 prospective, 1 retrospective</td>
<td>Retrospective series of 49 patients with cerebral venous thromboses presenting with headache, some of whom were given analgesics; prospective series of 35 similar patients</td>
<td>Pain relief/none (was not the primary measure in study)</td>
<td>Retrospective: 4/23 patients (who had pain relief recorded) had relief with “common analgesics”; prospective: 1/18 had full relief, 9/18 had partial relief</td>
<td>Design; not a predefined outcome measure, even in the prospective series</td>
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<tr>
<td>Abisaab et al&lt;sup&gt;14&lt;/sup&gt;</td>
<td>2004</td>
<td>Case report</td>
<td>1 postpartum patient with a bilateral carotid dissection</td>
<td>Pain relief/none</td>
<td>“Immediate” relief with subcutaneous sumatriptan</td>
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<tr>
<td>Leira et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>2001</td>
<td>Case report</td>
<td>1 case of spontaneous carotid dissection</td>
<td>Pain relief/none</td>
<td>“90%” relief of pain 2 h after a 50 mg oral dose of sumatriptan</td>
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<td>Pfadenhauer et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td>2006</td>
<td>Case series</td>
<td>3 patients with subarachnoid hemorrhage given sumatriptan</td>
<td>Pain relief/none</td>
<td>2 cases with subcutaneous sumatriptan and 1 with oral sumatriptan; all had partial pain relief</td>
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<td>Study</td>
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<tr>
<td>Rothrock17</td>
<td>2005</td>
<td>Case report</td>
<td>1 case of subarachnoid hemorrhage given sumatriptan</td>
<td>Pain relief/none</td>
<td>1 case with subarachnoid hemorrhage whose pain went from severe to mild after subcutaneous sumatriptan</td>
<td>Design</td>
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<tr>
<td>Wang et al18</td>
<td>2004</td>
<td>Case series</td>
<td>16 cases of dilated cyst of the cavum septi pellucidi</td>
<td>Pain relief/none</td>
<td>7/16 cases showed a &quot;fair response&quot; to indomethacin</td>
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<tr>
<td>US Headache Consortium22</td>
<td>2000</td>
<td>Retrospective review of literature from 1966-1998</td>
<td>Review of all English-language studies evaluating neuroimaging in the setting of nonacute headache</td>
<td>Summary recommendations</td>
<td>Recommendations: 1) neuroimaging should be considered in nonacute headache and unexplained neurologic findings (grade B); 2) insufficient evidence about neuroimaging in presence or absence of neurologic symptoms (grade C); 3) neuroimaging usually not warranted in migraine and normal examination (grade B); 4) insufficient evidence in tension-type headache (grade C); 5) insufficient evidence regarding CT or MRI in migraine and nonacute headache (grade C)</td>
<td>Design</td>
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<td>Study</td>
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<td>Intervention(s)/Test(s)/Modality</td>
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<td>Lledo et al24</td>
<td>1994</td>
<td>1 y prospective study</td>
<td>Inclusion: acute sudden-onset headache with no history, normal neurologic examination by neurologist; all patients had CT, if normal, LP performed; 3 mo follow-up</td>
<td>27 patients enrolled: 9 with subarachnoid hemorrhage, 1 with intraventricular hemorrhage, 1 with bacterial meningitis, 1 with viral meningitis, 15 unknown</td>
<td>No combination of findings identified patients with subarachnoid hemorrhage; CT findings positive in 4/9 patients with subarachnoid hemorrhage; neither altered mental status, neurologic examination, nor improving symptoms distinguished subarachnoid hemorrhage group</td>
<td>No exclusion criteria given; small sample size with no power analysis; patients followed for 3 mo; no angiograms performed to rule out unruptured aneurysm</td>
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<td>Harling et al25</td>
<td>1989</td>
<td>Prospective study of patients with thunderclap headache and normal brain CT and CSF results; of the 49 patients, 35 had subarachnoid hemorrhage</td>
<td>Follow-up at 18 mo</td>
<td>Subarachnoid hemorrhage at 18 mo follow-up; 8/14 had angiograms (all results negative)</td>
<td>Of the 14 patients with a negative initial evaluation, none had subarachnoid hemorrhage or sudden death at follow-up</td>
<td>Selection bias; small numbers; inclusion criteria not defined; not all patients had angiogram</td>
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<tr>
<td>Akpek et al26</td>
<td>1995</td>
<td>Retrospective study</td>
<td>CT imaging in headache; inclusion: no neurologic findings; exclusion: complaints of vision change, vertigo, dizziness, personality change, cancer</td>
<td>Cost-effectiveness of CT imaging in headache patients</td>
<td>592 patients (8-88 y); no patient with acute intracranial process was identified</td>
<td>Retrospective design; no formal neurologic examination; all exclusion criteria not reported</td>
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<td>Demaerel et al</td>
<td>1996</td>
<td>Prospective series</td>
<td>363 consecutive patients with chronic headache referred to radiology for CT with/without contrast; inclusion: normal neurologic examination; exclusion: vertigo, dizziness, migraine, epilepsy</td>
<td>Sensitivity of CT imaging in chronic headache population with normal neurologic examination</td>
<td>11 (3%) had a space-occupying lesion; none required emergency surgery</td>
<td>Did not evaluate acute headache population; selection bias</td>
<td>III</td>
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<td>Mitchell et al</td>
<td>1993</td>
<td>Prospective study of military ED and clinics</td>
<td>CT imaging in the headache patient; inclusion: headache of undetermined origin; exclusion: seizure, trauma, neoplasms, known etiology of headache</td>
<td>CT imaging sensitivity to detect significant intracranial findings</td>
<td>350 patients; 7 (2%) had significant findings (eg, tumor, subdural hematoma, subarachnoid hemorrhage, hydrocephalus, sinusitis); 27 had abnormal examination but normal CT imaging result; all patients with positive CT findings had abnormal physical or neurologic examination; 27 reported “worst headache of life”; only 1 had subarachnoid hemorrhage; unusual symptomatology (eg, “worst headache,” syncope, vomiting) did not predict positive CT findings on examination</td>
<td>Study performed by radiology; no protocol for referral; selection bias; although consecutive patients were referred from ED and clinics, it does not necessarily represent consecutive patients who presented to ED or clinics with headache</td>
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<td>Mills et al&lt;sup&gt;29&lt;/sup&gt;</td>
<td>1986</td>
<td>Prospective observational</td>
<td>ED patients having urgent CT imaging</td>
<td>Results of CT imaging in ED patient population</td>
<td>42 patients in headache subset (407 total patients); 21% had positive CT finding; only 1 patient had focal examination; 29% with “worst headache of life” had positive CT result (LP not provided)</td>
<td>Selection bias-enrollment dependent on house staff; neurologic examination by emergency medicine house staff; trauma patients included but percentage not reported</td>
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<td>Ramirez-Lassepas et al&lt;sup&gt;30&lt;/sup&gt;</td>
<td>1997</td>
<td>Retrospective review</td>
<td>15-mo review of patients with complaint of headache; random selection of 329 of 1,720 ED patients and 139 of hospitalized patients; 6 mo follow-up</td>
<td>4.2% ED patients evaluated for headache (1,859/44,080); 139 hospitalized; 3.8% had intracranial process (subarachnoid hemorrhage, tumor, intracranial hemorrhage, bacterial meningitis, cerebral infarction, herpes encephalitis)</td>
<td>Clinical findings and historical findings had a low positive predictive value but absence had a high negative predictive value; no association found between type of headache and pathologic entities; abnormal neurologic examination and headache had a 39% positive predictive value for intracranial process; acute onset, occipitonal location, and age older than 55 y were identified as clinical parameters associated with intracranial process</td>
<td>Selection process and inclusion/exclusion criteria not well described; no patient follow-up of patients discharged from ED; randomization process not described; hospitalized patients not described</td>
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<td>Kahn et al</td>
<td>1993</td>
<td>Retrospective</td>
<td>Comparison of CT imaging for nontraumatic headache in 2 centers in United States and Canada; inclusion: acute migraine or headache; exclusion: trauma or surgery</td>
<td>1,111 CT imaging examinations during 3-y period; 11% had acute intracranial process (e.g., hemorrhage, infarction, tumor); 18% had chronic process (e.g., old infarction, atrophy)</td>
<td>Study does not specifically address predictors of positive findings because population not well described; frequency highest in hospitalized patients and those &gt;40 y; proportion of positive findings in migraine group did not differ from other group</td>
<td>Did not provide clinical information that determined testing</td>
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<td>Duarte et al</td>
<td>1996</td>
<td>Prospective</td>
<td>100 consecutive patients with new headache occurring within 1 y of presentation; recruited from general practitioners; all patients had CT with/without contrast; all patients &gt;60 y had erythrocyte sedimentation rate</td>
<td>Prevalence of abnormal CT imaging findings in patients referred for new-onset headache</td>
<td>Although the study identified a large number of patients with intracranial process, it failed to identify those patients in need of imaging study in the ED; 80 patients had normal examination findings; 21 had intracranial neoplasms (13 with normal neurologic examinations); no combination of historical or physical findings excluded headache patients with intracranial process</td>
<td>Recruitment procedure biased, referral population not necessarily reflective of ED population; not specifically dealing with acute headache</td>
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### Evidentiary Table (continued).

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<td>Day and Raskin&lt;sup&gt;33&lt;/sup&gt;</td>
<td>1986</td>
<td>Case report</td>
<td>Angiography in a patient with thunderclap headache and normal brain CT and CSF results</td>
<td>Symptom relief after aneurysm surgery</td>
<td>I patient who had an aneurysm and diffuse vasospasm; the aneurysm was clipped; symptoms resolved</td>
<td>Single patient in whom symptoms may not have been related to the aneurysm</td>
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<tr>
<td>Linn et al&lt;sup&gt;35&lt;/sup&gt;</td>
<td>1994</td>
<td>Prospective cohort series of patients with thunderclap headache, and normal brain CT and CSF results</td>
<td>103 patients with thunderclap headache seen by Dutch general practitioners; 11% had subarachnoid hemorrhage; those with negative initial evaluations were followed for 1 y</td>
<td>No subarachnoid hemorrhage or sudden death at 1-y clinical follow-up</td>
<td>No patient not identified in the initial evaluation had subarachnoid hemorrhage or sudden death</td>
<td>Not all patients had a standard diagnostic evaluation (not all had CT); given study setting, may have limited external validity</td>
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<td>Wijdicks et al&lt;sup&gt;36&lt;/sup&gt;</td>
<td>1988</td>
<td>Retrospective analysis of a prospectively collected series of patients with thunderclap headache and normal brain CT and CSF results</td>
<td>Follow-up of patients for evidence of subarachnoid hemorrhage or sudden unexplained death; 6/71 had negative angiograms; none of the patients had subarachnoid hemorrhage</td>
<td>No subarachnoid hemorrhage or sudden death at (average) 3.3-y follow-up</td>
<td>No patient had subarachnoid hemorrhage or sudden death at follow-up</td>
<td>Design; nonstandard evaluation</td>
<td>III</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
<td>Outcome Measure/Criterion Standard</td>
<td>Results</td>
<td>Limitations/Comments</td>
<td>Class</td>
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<tr>
<td>Landtblom et al&lt;sup&gt;37&lt;/sup&gt;</td>
<td>2002</td>
<td>Prospective cohort series of patients with thunderclap headache and normal brain CT and CSF results</td>
<td>Study with 2 phases: Phase 1: 31 mo during which neurologist on call; Phase 2: 19 mo during which there was better coverage for incidence study</td>
<td>No subarachnoid hemorrhage or sudden death at 1-y clinical follow-up</td>
<td>No patient with a negative CT and CSF analysis at the first visit was later found to have subarachnoid hemorrhage at 12 mo follow-up</td>
<td>All patients examined by study neurologists; given study setting, may have limited external validity</td>
<td>II</td>
</tr>
<tr>
<td>DeLashaw et al&lt;sup&gt;45&lt;/sup&gt;</td>
<td>2005</td>
<td>Case review</td>
<td>Presentation of a single case of postpartum CVT and review of identification, management, and treatment</td>
<td>Case review</td>
<td>Review</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>English and Mulvey&lt;sup&gt;46&lt;/sup&gt;</td>
<td>2004</td>
<td>Case report</td>
<td>Report of arteriovenous malformation bleed in woman during induction of labor</td>
<td>Case report</td>
<td>Review</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
<td>Outcome Measure/Criterion Standard</td>
<td>Results</td>
<td>Limitations/Comments</td>
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<tr>
<td>Sidman et al&lt;sup&gt;60&lt;/sup&gt;</td>
<td>1996</td>
<td>Retrospective review</td>
<td>Reviewed all ED patients receiving third generation CT and LP for nontraumatic subarachnoid hemorrhage</td>
<td>140 patients identified with subarachnoid hemorrhage; sensitivity of CT in the diagnosis of nontraumatic subarachnoid hemorrhage when performed ≤12 h of symptom duration was 100% (80/80), and was 81.7% (49/60) after 12 h of symptom duration (95% CI 95%-100% and 69.5%-90.4%, respectively; ( P &lt; 0.0001 )); 11/140 had a negative CT and positive spinal fluid analysis, yielding an overall sensitivity of 92.1% (129/140)</td>
<td>Review</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>Shah et al&lt;sup&gt;53&lt;/sup&gt;</td>
<td>2003</td>
<td>Retrospective review</td>
<td>Reviewed all LP results (N=786) in hospital in attempt to describe traumatic attempt incidence</td>
<td>Incidence of traumatic taps 15% traumatic incidence; better rates in ED</td>
<td>Review</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
<td>Outcome Measure/Criterion Standard</td>
<td>Results</td>
<td>Limitations/Comments</td>
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<tr>
<td>Perry et al&lt;sup&gt;68&lt;/sup&gt;</td>
<td>2008</td>
<td>Prospective cohort study of alert patients presenting to 2 tertiary EDs with a chief complaint of nontraumatic headache</td>
<td>592 patients (61 with subarachnoid hemorrhage) in a study to test the accuracy of the diagnostic strategy of combined CT and LP to rule out a subarachnoid hemorrhage</td>
<td>Patients diagnosed with subarachnoid hemorrhage and patients with negative evaluation who did not have subarachnoid hemorrhage on follow-up</td>
<td>All 61 patients with subarachnoid hemorrhage were found by the combined diagnostic strategy: CT (55 patients) or LP (6 patients)</td>
<td>Unable to follow up 20% of patients (though strict measures were taken that make it unlikely those patients had a subsequent subarachnoid hemorrhage); 1 patient later was found to have an asymptomatic aneurysm not thought to have caused the original headache</td>
<td>II</td>
</tr>
<tr>
<td>Foot and Staib&lt;sup&gt;69&lt;/sup&gt;</td>
<td>2001</td>
<td>Retrospective case review</td>
<td>Reviewed all cases with subarachnoid hemorrhage–type symptoms who had CT and LP</td>
<td>Role of CSF xanthochromia to alter outcome and management</td>
<td>Only 1/189 had CT/LP positive but significant variation on how LP interpreted within their institution</td>
<td>Retrospective; criteria for study entry were LP and having CT; some may have just had CT, which could miss cases; considerable management variation within institution, generalizability questioned</td>
<td>III</td>
</tr>
<tr>
<td>O’Neill et al&lt;sup&gt;70&lt;/sup&gt;</td>
<td>2005</td>
<td>Retrospective study of acute headache patients presenting to an ED and for whom a brain CT scan was performed</td>
<td>127 patients identified of whom 11 were excluded because of incomplete record retrieval; 19 patients had subarachnoid hemorrhage</td>
<td>Patients diagnosed with subarachnoid hemorrhage by CT scan versus LP</td>
<td>Of the 116 included patients, 81 had a normal CT; 40 of those patients (49%) had LP performed; 6 patients had xanthochromia, all of whom had angiography; 4 were normal; 2 showed aneurysms</td>
<td>Half of eligible patients for LP did not have LPs done; half of patients had no diagnosis on discharge</td>
<td>III</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
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<tr>
<td>Boesiger and Shiber</td>
<td>2005</td>
<td>Retrospective chart review</td>
<td>Identified ED headache patients having both CT (fifth generation) and LP to estimate local imaging sensitivity and specificity for subarachnoid hemorrhage</td>
<td>Disagreement between CT and LP</td>
<td>N=177; no missed subarachnoid hemorrhage cases in CT-negative patients; suggests newer CT imaging more sensitive than earlier scanners</td>
<td>Retrospective review; selection bias (CT but patient refused LP); missed cases</td>
<td>III</td>
</tr>
<tr>
<td>Bynny et al</td>
<td>2008</td>
<td>Retrospective chart review</td>
<td>149 patients presenting to or transferred to an ED with nontraumatic subarachnoid hemorrhage to find CT sensitivity; 4-slice, 4-detector CT scanner was used</td>
<td>Percentage of patients whose CT scans were negative but who were diagnosed with LP</td>
<td>139/149 patients with nontraumatic subarachnoid hemorrhage had positive CT scan results; 10/149 were diagnosed by LP; in less severely affected patients (normal mental status) 78/87 patients had a positive CT result (sensitivity of 90%)</td>
<td>Referral tertiary care population; some patients with missing LP data</td>
<td>III</td>
</tr>
<tr>
<td>Duffy</td>
<td>1969</td>
<td>This appears to be a retrospective review of patients found to have midbrain and medullary compression syndromes after an LP</td>
<td>LP</td>
<td>Midbrain and medullary compression syndrome</td>
<td>10 of 30 patients stopped breathing or developed unequal pupils while the needle was still in place or shortly after it was removed; 15 of the 30 patients had marked deterioration within 24 h of the procedure; all 30 patients in this report had significant clinical findings such as a focal neurologic examination, progressive mental status changes, papilledema, “meningitic symptoms,” or abnormal cranial radiograph results</td>
<td>Study design not described; no analysis for bias selection addressed; LP in patients with no complications not included; the relative contributions of the LP versus the natural disease course to the patient’s clinical deterioration is not known</td>
<td>X</td>
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</tbody>
</table>
### Evidentiary Table (continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>Intervention(s)/Test(s)/Modality</th>
<th>Outcome Measure/Criterion Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duffy</td>
<td>1982</td>
<td>It is unclear whether this is a retrospective study or a 2-year prospective observational study; inclusion: patients considered to have a complication caused by the LP had to have clinical deterioration while the spinal needle was still in place; exclusion: patients whose clinical status changed after the LP was performed</td>
<td>LP</td>
<td>LP complication while spinal needle is in place</td>
</tr>
</tbody>
</table>

74 patients included in analysis; 44 had LP before CT scan; 7 of the 44 patients deteriorated while LP was being performed; all were drowsy, confused, or had “mild” hemiparesis before performing the procedure; 6 of the 7 patients had structural evidence of herniation in the operating room or at autopsy; 4 of the 7 died and 3 of the 7 had long-term neurologic sequelae; 12 patients had hemispheric shift on CT scan, 5 underwent LP, and 3 of the 5 deteriorated subsequent to LP; conclusion: the risk of herniation is significant in patients who undergo spinal tap and have an intracranial hematoma with a hemispheric shift

Limitations/Comments: Unclear study design; there was no standardization in the management of these patients; LP in patients with no neurologic signs were not included

Class: III
<table>
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<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>Intervention(s)/Test(s)/Modality</th>
<th>Outcome Measure/Criterion Standard</th>
<th>Results</th>
<th>Limitations/Comments</th>
<th>Class</th>
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</thead>
<tbody>
<tr>
<td>French and Glasgow 78</td>
<td>1985</td>
<td>Retrospective chart review of 109 patients admitted for subarachnoid hemorrhage; inclusion: patients who were drowsy, confused, or had “mild” hemiparesis; exclusion: stupor, coma, or “significant” hemiparesis</td>
<td>Lumbar puncture</td>
<td>Mild hemiparesis, drowsiness, confusion</td>
<td>One of the 70 patients, a patient with subarachnoid hemorrhage, deteriorated after the LP and died after 12 days, leading to the conclusion that herniation, even in the neurologically symptomatic patient, is uncommon</td>
<td>Retrospective study design; timing of CT scans was not reported; no long-term outcome data reported</td>
<td>III</td>
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<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
<td>Outcome Measure/Criterion Standard</td>
<td>Results</td>
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<tr>
<td>Zisfein and Tuchman</td>
<td>1988</td>
<td>Prospective observational design during a 3-y period; inclusion: patients requiring a LP to rule out meningitis who subsequent to procedure, are found within 1 wk to have a space-occupying lesion by CT scan; exclusion: patients in whom an LP is done but no intracranial mass lesion is documented by CT scan</td>
<td>LP</td>
<td>Neurologic deterioration in patients receiving LP</td>
<td>38 patients were included; 34 of the 38 patients’ CT scans revealed mass effect; the 4 remaining studies were of poor quality and could not be evaluated for this finding; 37 of the 38 patients were the same or improved at 48 h after the LP; 1 patient with fixed dilated pupils and absent corneal reflexes before the LP subsequently died; 3 patients who were worsening before the LP continued to do poorly but returned to baseline; herniation is uncommon in the setting of intracranial mass lesions even in the presence of mass effect</td>
<td>Indications for suspicion of meningitis are not reported; without a prespinal tap CT scan there is no way to know whether the shift on CT scan resulted from the LP; no patients suspicious of having subarachnoid hemorrhage are included; heterogeneous group of CNS lesions</td>
<td>III</td>
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</table>
### Evidentiary Table (continued).

<table>
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<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>Intervention(s)/Test(s)/Modality</th>
<th>Outcome Measure/Criterion Standard</th>
<th>Results</th>
<th>Limitations/Comments</th>
<th>Class</th>
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<tbody>
<tr>
<td>Gopol et al</td>
<td>1999</td>
<td>Prospective cohort during an 18-mo period</td>
<td>Preselected medical history and physical examination data were collected on all patients who were determined to need a LP; internal medicine resident (with ED attending supervision) suspicion that a patient would have a CT finding that would contraindicate LP was also documented before performance of the CT scan</td>
<td>Physician pretest ability to predict the likelihood of a CT finding that would contraindicate dural puncture</td>
<td>111 patients were assessed; reasons for LP: rule out subarachnoid hemorrhage (42.3%), rule out meningitis (36.9%), and other (20.7%); 15.3% (15) had documented lesions; 2.7% (3) had contraindications to LP (a lesion with mass effect); physicians were able to predict all patients who were found to have contraindications to LP; altered mental status, papilledema, and focal neurologic examination increased the likelihood of an abnormal CT finding; absence of historical or physical findings had a negative likelihood ratio of 0 for finding new CNS pathology; supports the notion that patients without focal neurologic findings, signs of increased intracranial pressure, or altered mental status are unlikely to have radiologic findings that contraindicate LP</td>
<td>Heterogeneous patient population; small number of patients with disease</td>
<td>II</td>
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<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
<td>Intervention(s)/Test(s)/Modality</td>
<td>Outcome Measure/Criterion Standard</td>
<td>Results</td>
<td>Limitations/Comments</td>
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<tr>
<td>Raps et al⁸⁴</td>
<td>1993</td>
<td>Retrospective chart review of patients presenting to a tertiary care center with unruptured intracranial aneurysm</td>
<td>54 of 111 patients had acute symptoms; 7 presented with a thunderclap headache; all had at least transient neurologic deficits</td>
<td>Symptoms thought to be due to unruptured aneurysms</td>
<td>7 patients presented with an acute severe headache probably related to the unruptured aneurysm</td>
<td>Study design; selection bias (tertiary referral center)</td>
<td>III</td>
</tr>
<tr>
<td>Witham and Kaufmann⁸⁵</td>
<td>2000</td>
<td>Case report</td>
<td>1 patient with a 13 mm unruptured aneurysm with normal CT and a traumatic LP</td>
<td>Findings at surgery</td>
<td>Single case of patient with symptomatic aneurysm and normal CT result but a traumatic LP (high RBC count with no xanthochromia)</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>McCarron and Choudhari⁸⁶</td>
<td>2005</td>
<td>Case report</td>
<td>Surgery in a patient with thunderclap headache with negative findings on standard workup</td>
<td>Findings at surgery</td>
<td>Single case of patient with symptomatic aneurysm and negative CT and LP results</td>
<td>Design; CSF not tested until 7 days after onset of headache</td>
<td>III</td>
</tr>
<tr>
<td>Hughes⁸⁷</td>
<td>1992</td>
<td>2 case reports</td>
<td>2 patients with thunderclap headache and negative CT findings (1 who also had negative LP findings)</td>
<td>Findings at angiography 2 wk after onset of headache</td>
<td>2 cases of (symptomatic but unruptured) aneurysm found after negative evaluations</td>
<td>Design</td>
<td>III</td>
</tr>
<tr>
<td>Carstairs et al⁹⁰</td>
<td>2006</td>
<td>Prospective cohort series</td>
<td>116 patients with thunderclap headache enrolled, 106 completed the study</td>
<td>Findings on digital angiogram</td>
<td>6 of the 116 patients had aneurysms by CT angiography</td>
<td>Aneurysms found could have been incidental; 3 of the 6 had abnormal CT or LP results; 1 other was a false positive (had negative formal angiogram)</td>
<td>II</td>
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</tbody>
</table>

CI, Confidence interval; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; CVT, cerebral venous thrombosis; ED, emergency department; h, hour; LP, lumbar puncture; mg, milligram; mm, millimeter; mo, month; MRI, magnetic resonance imaging; RBC, red blood cell; US, United States; wk, week; y, year.
Appendix A. Literature classification schema.*

<table>
<thead>
<tr>
<th>Design/Class</th>
<th>Therapy</th>
<th>Diagnosis</th>
<th>Prognosis</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Randomized, controlled trial or meta-analyses of randomized trials</td>
<td>Prospective cohort using a criterion standard</td>
<td>Population prospective cohort</td>
</tr>
<tr>
<td>2</td>
<td>Nonrandomized trial</td>
<td>Retrospective observational</td>
<td>Retrospective cohort Case control</td>
</tr>
<tr>
<td>3</td>
<td>Case series Case report Other (eg, consensus, review)</td>
<td>Case series Case report Other (eg, consensus, review)</td>
<td>Case series Case report Other (eg, consensus, review)</td>
</tr>
</tbody>
</table>

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing ≥2 interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

<table>
<thead>
<tr>
<th>Downgrading</th>
<th>Design/Class</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>I</td>
</tr>
<tr>
<td>1 level</td>
<td>II</td>
</tr>
<tr>
<td>2 levels</td>
<td>III</td>
</tr>
<tr>
<td>Fatally flawed</td>
<td>X</td>
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