5-1-2006

# Computed tomographic angiography for the evaluation of aneurysmal subarachnoid hemorrhage.

Shaun D Carstairs

David A Tanen

Timothy D Duncan

Olaf B Nordling

John E Wanebo
john.wanebo@barrowbrainandspine.com

*See next page for additional authors*

## Authors

Shaun D Carstairs, David A Tanen, Timothy D Duncan, Olaf B Nordling, John E Wanebo, Thomas R Paluska, Nicholas Theodore, and Robert H Riffenburgh

# Computed Tomographic Angiography for the Evaluation of Aneurysmal Subarachnoid Hemorrhage

Shaun D. Carstairs, MD, David A. Tanen, MD, Timothy D. Duncan, MD, Olaf B. Nordling, MD, John E. Wanebo, MD, Thomas R. Paluska, MD, Nicholas Theodore, MD, Robert H. Riffenburgh, PhD

## Abstract

***Objectives:*** Computed tomography (CT) followed by lumbar puncture (LP) is currently the criterion standard for diagnosing subarachnoid hemorrhage (SAH) in the emergency department (ED); however, this is based on studies involving a limited number of patients. The authors sought to assess the ability of CT angiography (CTA), a new diagnostic modality, in conjunction with CT/LP to detect SAH.

***Methods:*** Consecutive patients presenting to the ED with symptoms concerning for SAH were approached. All patients had an intravenous catheter placed and underwent a noncontrast head CT followed by CTA. Patients whose CT did not reveal evidence of SAH or other pathology underwent LP in the ED. CTAs were read within 24 hours by a neuroradiologist blinded to the patient's history.

***Results:*** A total of 131 patients were approached, 116 were enrolled, and 106 completed the study. In six of 116 patients (5.1%), aneurysm was found on CTA with normal CT and positive findings on LP; three had a positive CTA with normal CT and LP findings (one of which had a negative cerebral angiogram), and there was one false-positive CTA. Follow-up of all 131 patients showed no previously undiagnosed intracranial pathology. In this patient population, 4.3% (5/116) were ultimately found to have an SAH and/or aneurysm.

***Conclusions:*** In this pilot study, CTA was found to be useful in the detection of cerebral aneurysms and may be useful in the diagnosis of aneurysmal SAH. A larger multicenter study would be useful to confirm these results.

ACADEMIC EMERGENCY MEDICINE 2006; 13:486–492 

**Keywords: computed tomography, CT angiography, subarachnoid hemorrhage, SAH, aneurysm**

From the Departments of Emergency Medicine (SDC, DAT, TRP), Radiology (TDD, OBN), Neurosciences (JEW, NT), and Clinical Investigation (RHR), Naval Medical Center San Diego, San Diego, CA.

Dr. Paluska is currently with the Emergency Medicine Department, National Naval Medical Center, Bethesda, MD, and Dr. Theodore is currently with the Division of Neurosurgery, Barrow Neurological Institute, Phoenix, AZ.

Received November 14, 2005; revision received December 9, 2005; accepted December 14, 2005.

The Chief, Bureau of Medicine and Surgery, Navy Department, Washington, DC, Clinical Investigation Program, sponsored this report #S-01-131 as required by NSHSBETHINST 6000.41B.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. government.

Address for correspondence: Shaun D. Carstairs, MD, Department of Emergency Medicine, Naval Medical Center San Diego, 34-800 Bob Wilson Drive, San Diego, CA 92134-5000. Fax: 619-532-5972; e-mail: shaunc@yahoo.com.

Patients with headache account for 1%–2% of visits to the emergency department (ED).[1–3] Most have primary headache disorders (such as migraine and tension-type headaches) that are not life threatening; however, within this group of patients, a subgroup of approximately 1%–4% has a nontraumatic subarachnoid hemorrhage (SAH), which can represent a catastrophic event.[1–3] The annual incidence of nontraumatic SAH is believed to range from approximately 11 to 25 per 100,000 population in the United States and results in at least 25,000 cases annually.[1–4] Early detection is critical because as many as 25% of patients may die within 24 hours, and the three-month mortality rate has been estimated to be as high as 50% without early definitive treatment.[1–5]

A total of 20%–50% of patients with documented SAH report a distinct, unusually severe headache in the days or weeks before the index episode of bleeding.[6–9] The current standard of care in the ED evaluation of patients who present with a "thunderclap" headache or "the


ISSN 1069-6563
PII ISSN 1069-6563583

doi: 10.1197/j.aem.2005.12.010

worst headache of my life" is to rule out SAH. This workup begins with noncontrast computed tomography (CT) of the head, which has been reported to be 92%–100% sensitive in the detection of SAH depending on the timing of the CT.[10,11] Because of the potentially devastating outcomes associated with SAH, if the CT is negative, a lumbar puncture (LP), historically the criterion standard for the detection of SAH, is performed. The potential of spectrum bias (variation of sensitivity and specificity depending on the population tested) also arises, because both CT and LP easily identify the patient with a large bleed but may have difficulty identifying a patient who has had a sentinel bleed.[4,12–15]

In cases in which both the CT and the LP results are normal, the patient is assumed not to have an SAH.[12–17] This assumption is based on accumulated experience and several small studies that have followed up clinical outcomes in patients with "thunderclap" headache and negative CT and LP findings. One study examined the outcomes of 71 such patients for an average of 3.5 years and found no untoward events (hemorrhage or sudden death); the largest of these studies found no adverse events in 137 patients at 12 months.[18–21]

Another modality that theoretically should be useful in the diagnosis of a nontraumatic SAH would be cerebral angiography. However, although it is considered the criterion standard in defining anatomy, no randomized controlled trials have compared CT/LP with cerebral angiography because of the invasive nature of the latter procedure,[5,18,22,23] the complication rate of which has been reported to be between 0.25% and 1%.[18] Recently, it has been suggested that CT angiography (CTA), a noninvasive means of defining cerebral anatomy, may improve detection of aneurysmal SAH in patients presenting with severe, acute-onset headache.[22–26] It is not a substitute for digital subtraction angiography (DSA) mainly due to the fact that the contrast in CTA is not injected intra-arterially and thus cannot provide physiologic data on the arterial, capillary, and venous phases that DSA provides. However, CTA has several advantages over conventional angiography in that it is faster, is easier to obtain, and does not require dedicated angiography staff. It is also less invasive and poses a lower risk of adverse effects such as stroke. We proposed to study this novel approach in conjunction with CT/LP in all patients presenting to the ED with a "thunderclap" headache or "the worst headache of my life." We hypothesized that the addition of CTA to the workup of these patients would improve the detection of aneurysmal SAH.

## METHODS

### Study Design

This was a prospective, controlled pilot study designed to assess the ability of CTA, in conjunction with CT/LP, to diagnose SAH in adult ED patients presenting with a chief complaint of headache concerning for SAH. The medical center's institutional review board for protection of human subjects approved the study. Written informed consent was obtained from all participants; if the patient was unable to give written consent, a family member or legal guardian was asked to provide written consent.

### Study Setting and Population

The study was conducted in the ED of a tertiary care medical center that serves active-duty and retired military personnel and their beneficiaries and has an annual census of 46,000 persons. Consecutive patients aged 18 years or older were eligible if they presented to the ED with one of the following: 1) complaint of "the worst headache of my life" or "thunderclap" headache (sudden onset of severe headache over 60 seconds or less), 2) sudden-onset headache different in quality and intensity from previous headaches, or 3) sudden-onset headache associated with altered mental status, loss of consciousness, or neurologic deficits.

Patients were excluded from enrollment if they met any of the following criteria: history of an allergic reaction to contrast dye or iodine allergy, history of reactive airway disease that necessitated daily medication, or evidence of renal insufficiency as determined by a measured serum creatinine level $\geq$1.4 mg/dL.

### Study Protocol

After obtaining informed consent, patients eligible for the study were enrolled. Patients had an 18-gauge (or larger) catheter placed in an upper extremity vein and were treated with analgesics according to the preference of their treating physician. Patients underwent a noncontrast head CT using a GE Lightspeed multidetector CT scanner (GE Healthcare, Waukesha, WI), with 3-mm cuts through the posterior fossa and 5-mm cuts through the rest of the brain, that was read by the on-call radiologist. Immediately following the CT, CTA was performed on the same scanner by injecting 100 mL Visipaque (iodixanol 320 mg/mL; GE Healthcare) at a rate of 4 mL/s via an 18-gauge (or larger) catheter placed in the upper extremity. All CTAs were scanned in 2.5-mm cuts from the inner table of the skull vertex to the C1/C2 level. Three-dimensional rotational reconstructions of vascular anatomy could later be performed from these cuts as deemed necessary by a neuroradiologist.

If the CT did not reveal evidence of SAH or other intracranial pathology (e.g., mass, hydrocephalus, cerebral edema), the patient underwent LP in the ED. Cerebrospinal fluid was obtained and analyzed for cell count (tubes 1 and 4), protein level, glucose level, and microbiologic studies. Samples were centrifuged and screened for xanthochromia by laboratory technicians using visual observational methods as previously described.[27] Based on previous studies,[28] we determined positive results indicative of SAH to be 1) absence of a decrement in red blood cells of more than 25% between the first and fourth tubes or 2) evidence of xanthochromia.

If either the CT or the LP result was positive, the patient was presumed to have SAH, and urgent neurologic consultation was obtained. The CTA was made available to the treating neurosurgeon on an emergent basis. All CTAs were read within 24 hours of the study by a board-certified neuroradiologist. All patients with CT, CTA, or LP results concerning for SAH and/or aneurysm underwent confirmatory conventional cerebral DSA for aneurysm sourcing at the discretion of the neurosurgeon. DSA was not used as a criterion standard for all patients because of the inherent small but finite risk of adverse effects, reported to be 1.8% in a recent meta-analysis.[29] Based on current neurosurgical practices, an aneurysm detected on CTA in a patient presenting with symptoms concerning for SAH was viewed as equivalent to the findings of an SAH on CT/LP.[30–34]

To ensure reproducibility of results, all noncontrast head CTs and CTAs were reread in a blinded fashion by a board-certified neurosurgeon and two board-certified neuroradiologists between three months and 24 months after the patient's presentation.

### Measurements

Information collected included patient demographic characteristics, time of headache onset, time of ED presentation, headache description, associated symptoms, vital signs, neurologic examination findings, and results of CT, CTA, and LP. Data were collected by the treating physician on standardized data collection forms, and results were entered into an Excel spreadsheet (Microsoft Corp., Redmond, WA).

### Data Analysis

κ values were calculated to measure interobserver agreement among the three blinded CTA readers. Statistical analysis (including κ values and patient characteristic data) was performed using SPSS 10.1 for Windows (SPSS Inc., Chicago, IL).

## RESULTS

Between July 2002 and July 2004, 131 patients were screened for enrollment. Fifteen patients refused enrollment, so 116 patients were enrolled in the study. A total of 106 patients completed the study; six were found to have evidence of aneurysm/SAH on CTA. Five of the six were subsequently confirmed to have evidence of an aneurysm by DSA, whereas one had normal findings on DSA (Table 1). Ten patients did not complete the study: five refused LP, one did not have LP performed due to an elevated international normalized ratio, one did not undergo CTA because of an elevated creatinine level that was discovered after enrollment, one did not undergo CTA due to miscommunication with the CT technician, and two were found to have evidence of other intracranial pathology on CT that the treating physician believed obviated the need for CTA (Figure 1). All of these patients were followed up at one year and were alive without evidence of SAH.

Baseline data, including demographic characteristics, headache time of onset, time of ED presentation, headache description, associated symptoms, vital signs, and findings on neurologic examination, are shown in Table 2. Figure 2 shows two examples of aneurysms found using CTA, and Figure 3 shows the one false-positive CTA that occurred during the course of this study. Ultimate diagnoses were recorded on all patients and are listed in Table 3. No adverse events (i.e., contrast reactions) occurred as a result of the CTA. The κ value among the three blinded readers was 0.944, indicating excellent interobserver agreement.

## DISCUSSION

The relatively new diagnostic modality of CTA may be a useful adjunct in the diagnosis of aneurysmal SAH due to its rapidity, ease of obtainability, and minimally invasive nature as compared with conventional angiography. In this pilot study, CTA was found to be useful for diagnosing aneurysms in patients presenting to the ED with thunderclap headache; indeed, two patients with normal findings on CT/LP were subsequently found to have evidence of aneurysm on CTA. Additionally, CTA was found to be useful in the diagnosis of other (non-SAH) causes of headache, including venous sinus thrombosis, ischemic stroke, and arteriovenous malformation.

In our study, CTA appeared to increase the rate of detection of SAH/aneurysm when used in conjunction with CT/LP. In our small study of 116 patients, at least

Table 1
Characteristics of Patients with Positive CTA Findings

| Age (y) | Gender | CT Results | LP Results | CTA Results | Conventional Angiography Results | Disposition |
|---|---|---|---|---|---|---|
| 71 | Female | Normal | Xanthochromia | 3-mm internal carotid artery wide neck blister aneurysm | Aneurysm confirmed | Surgical clipping; suffered nontraumatic subdural hematoma 24 months status post clipping |
| 48 | Female | Normal | Normal | 7-mm MCA aneurysm | Aneurysm confirmed | Surgical clipping |
| 56 | Female | SAH | Not performed | 5-mm bilobed ACOM aneurysm | Aneurysm confirmed | Surgical clipping |
| 38 | Female | Normal | Normal | 7-mm MCA aneurysm at trifurcation | Aneurysm confirmed | Refused surgical clipping or coiling |
| 44 | Male | Normal | Positive (433 to 390 red blood cells) | 3-mm ACOM aneurysm | Aneurysm confirmed | Surgical clipping |
| 38 | Male | Normal | Normal | "Rounded opacity" in ACOM | Normal (false-positive CTA) | No adverse outcome |

CT = computed tomography; LP = lumbar puncture; CTA = computed tomographic angiography; MCA = middle cerebral artery; SAH = subarachnoid hemorrhage; ACOM = anterior communicating artery.

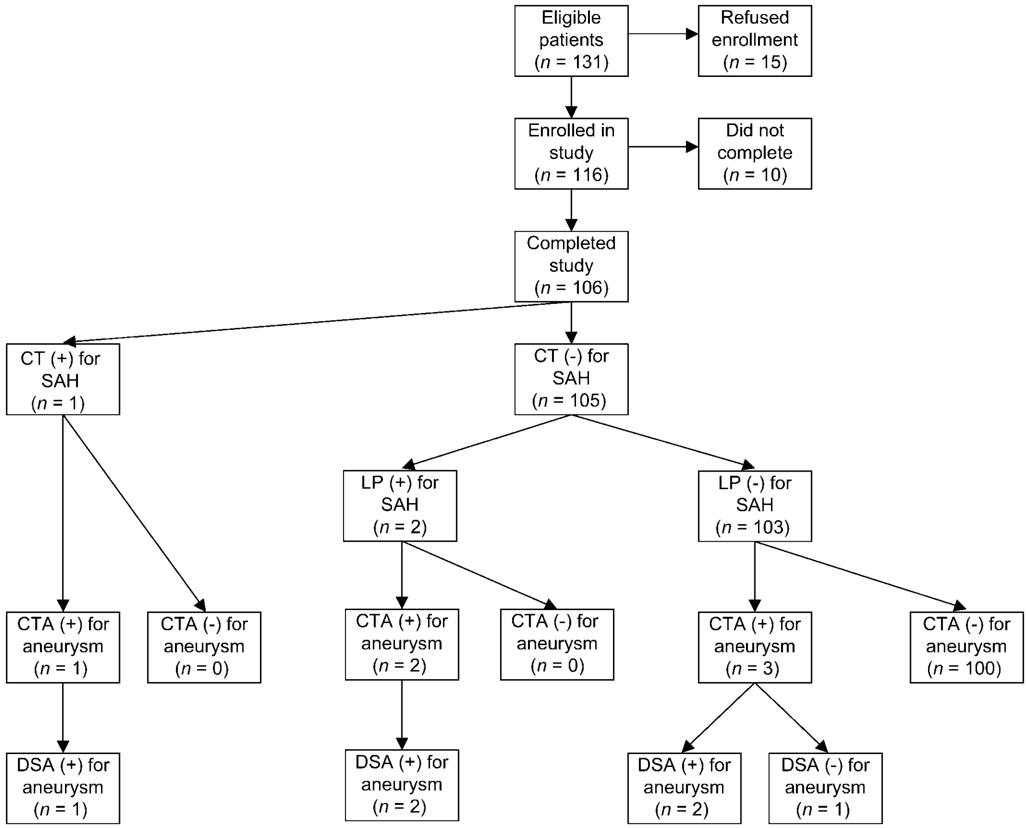


**Figure 1. Patient study flow diagram.**

Table 2
Patient Characteristics

| Baseline Data | All Patients ($N$ = 116) | Aneurysm/ Subarachnoid Hemorrhage ($n$ = 5) |
|---|---|---|
| Gender (%) | | |
| Male | 49 (42.2) | 1 (20) |
| Female | 67 (57.7) | 4 (80) |
| Age (y), mean ± SD | 38.8 ± 14.8 | 53.3 ± 13.9 |
| Time from headache onset to presentation (h), mean ± SD | 38.4 ± 46.8 | 39.9 ± 35.9 |
| Associated symptoms (%) | | |
| Nausea | 67 (57.7) | 4 (80) |
| Photophobia | 58 (50.0) | 4 (80) |
| Stiff neck | 37 (31.9) | 3 (60) |
| Blurred vision | 6 (5.2) | 2 (40) |
| Vital signs at ED triage, mean ± SD | | |
| Systolic blood pressure (mm Hg) | 133.8 ± 22.3 | 142.7 ± 21.2 |
| Diastolic blood pressure (mm Hg) | 80.8 ± 13.9 | 90.7 ± 14.4 |
| Heart rate (beats/min) | 80.3 ± 17.6 | 68.3 ± 4.9 |
| Temperature (°C) | 36.5 ± 1.6 | 36.6 ± 0.6 |
| Examination findings (%) | | |
| Nuchal rigidity | 17 (14.7) | 0 (0) |
| Focal neurologic deficit | 6 (5.2) | 1 (20) |
| Altered mental status | 3 (2.6) | 0 (0) |

two additional suspected cases of SAH were found that might have been missed by CT/LP. Additionally, CTA may help with defining the affected anatomy before surgery. With the increasing resolution that CTA provides, a growing number of institutions are treating intracranial aneurysms on the basis of CTA imaging alone in a majority of their patients.[35] Hoh et al. have described a cohort of 223 patients in whom CTA was used safely and effectively as the sole imaging modality in 82% of patients for planning surgical repair or endovascular coiling.[36]

CTA is not without its risks. Although our protocol used nonionic iso-osmolar contrast to minimize the risk of contrast-induced nephropathy, there is a theoretical risk of contrast-induced nephropathy with all types of intravenous contrast material. To our knowledge, none of our patients experienced this complication, and all were doing well at one-year follow up. In addition, a recent retrospective review of 59 patients found no significant risk of contrast-induced nephropathy in patients undergoing CTA with nonionic contrast.[37] There may also be a small but nonquantifiable increase in lifetime cancer risk from the additional radiation during CTA.[38]

## LIMITATIONS

Our study has several limitations. This was a pilot study with a relatively small number of true positives and total patients. The study was performed at a single site and in a specific population (military members, their

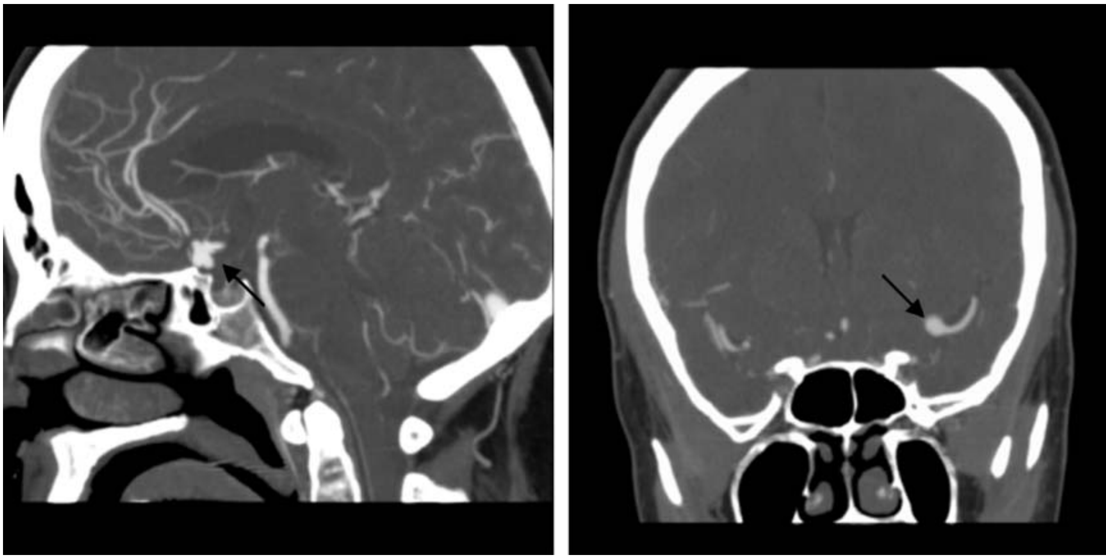

**Figure 2.** Examples of aneurysms found with CTA (arrows).

families, and military retirees), potentially limiting the generalizability of the results. Screening for xanthochromia was performed using visual observation rather than spectrophotometry, which is generally agreed to be more accurate.

Additionally, for the purposes of our study, we treated the presence of either SAH or aneurysm as equivalent. In those patients with negative findings on CT/LP who were found to have an aneurysm on CTA, it is difficult, if not impossible, to show a definitive cause-and-effect relationship between the patients' symptoms and the aneurysm found on CTA. Although we cannot be certain that the aneurysm was the cause of the headache in these patients, a systematic review by Rinkel et al. demonstrated that "symptomatic" aneurysms (those aneurysms found in the course of a workup for headache or other symptoms concerning for SAH) have a relative risk of rupture of 8.3 compared with "asymptomatic" aneurysms (those aneurysms found incidentally in the absence of symptoms such as headache).[39] It is currently accepted neurosurgical practice that aneurysms presenting with an acute onset of symptoms should be treated.[30–34] We are not suggesting that all aneurysms found incidentally in all patients should be treated. However, given the high rate of rupture of aneurysms found in the course of a workup for headache, the presence of an aneurysm on CTA in our study patient population should prompt urgent neurosurgical consultation for consideration of treatment. The detection of aneurysm on CTA, while not proof of headache etiology, may be an index of SAH in the right clinical setting.

## CONCLUSIONS

Our results suggest that CTA in conjunction with CT/LP may be useful in the workup of aneurysmal SAH, especially in patients who, by history and physical examination, are believed to be at high risk for aneurysm based

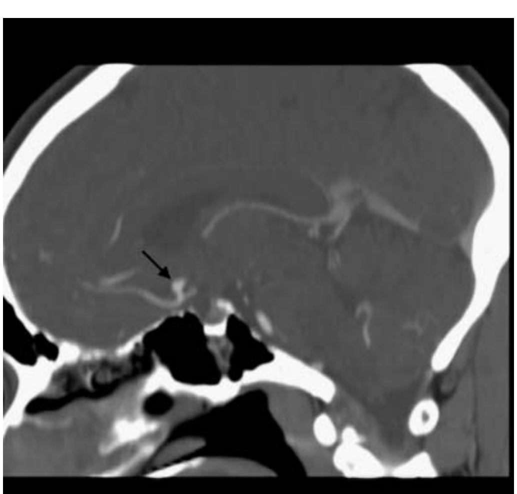

**Figure 3.** False-positive CTA (arrow).

Table 3
Final Diagnoses

| Diagnosis | No. of Patients |
|---|---|
| Aneurysm/subarachnoid hemorrhage | 5 |
| Meningitis | 7 |
| Sinusitis | 7 |
| Arteriovenous malformation | 1 |
| Cerebellar hematoma | 1 |
| Astrocytoma | 1 |
| Subdural hematoma/arachnoid cyst | 1 |
| Occipital infarct | 1 |
| Cerebellar infarct | 1 |
| Hypertensive emergency | 1 |
| Preeclampsia | 1 |
| Pseudotumor cerebri | 1 |
| Transverse sinus thrombosis | 1 |
| Temporal arteritis | 1 |
| Headache not otherwise specified | 86 |
| Total | 116 |

on presentation. However, a multicenter trial with larger numbers of patients would be useful to confirm our findings. Although our initial results are promising, we cannot currently recommend a change in the standard of care (CT/LP) based on this pilot study.

## References


1. Edlow JA, Caplan LR. Avoiding pitfalls in the diagnosis of subarachnoid hemorrhage. N Engl J Med. 2000; 342:29–36.
2. Sidman R, Connolly E, Lemke T. Subarachnoid hemorrhage diagnosis: lumbar puncture is still needed when the computed tomography scan is normal. Acad Emerg Med. 1996; 3:827–31.
3. Field AG, Wang E. Evaluation of the patient with nontraumatic headache: an evidence-based approach. Emerg Med Clin North Am. 1999; 17: 127–52.
4. Adams HP, Kassell NF, Torner JC, Sahs AL. CT and clinical correlations in recent aneurysmal subarachnoid hemorrhage: a preliminary report of the cooperative aneurysm study. Neurology. 1983; 33: 981–8.
5. Vermeulen M. Subarachnoid hemorrhage: diagnosis and treatment. J Neurol. 1996; 243:496–501.
6. Okawara SH. Warning signs prior to rupture of an intracranial aneurysm. J Neurosurg. 1973; 38:575–80.
7. Leblanc R. The minor leak preceding subarachnoid hemorrhage. J Neurosurg. 1987; 66:35–9.
8. Juvela S. Minor leak before rupture of an intracranial aneurysm and subarachnoid hemorrhage of unknown etiology. Neurosurgery. 1992; 30:7–11.
9. Jakobsson KE, Saveland H, Hillman J, et al. Warning leak and management outcome in aneurysmal subarachnoid hemorrhage. J Neurosurg. 1996; 85: 995–9.
10. Perry JJ, Stiell IG, Wells GA, et al. The sensitivity of computed tomography for the diagnosis of subarachnoid hemorrhage in ED patients with acute headache [abstract]. Acad Emerg Med. 2004; 11:435–6.
11. Boesiger BM, Shiber JR. Subarachnoid hemorrhage diagnosis by computed tomography and lumbar puncture: are fifth generation CT scanners better at identifying subarachnoid hemorrhage? J Emerg Med. 2005; 29:23–7.
12. Hoffman JR. Computed tomography for subarachnoid hemorrhage: what should be made of the "evidence"? Ann Emerg Med. 2001; 37:345–9.
13. van der Wee N, Rinkel GJ, Hasan D, van Gijn J. Detection of subarachnoid hemorrhage on early CT: is lumbar puncture still needed after a negative scan? J Neurol Neurosurg Psychiatry. 1995; 58:357–9.
14. Morgenstern LB, Luna-Gonzales H, Huber JC, et al. Worst headache and subarachnoid hemorrhage: prospective, modern computed tomography and spinal fluid analysis. Ann Emerg Med. 1998; 32: 297–304.
15. Sames TA, Storrow AB, Finkelstein JA, Magoon MR. Sensitivity of new-generation computed tomography in subarachnoid hemorrhage. Acad Emerg Med. 1996; 3:16–20.
16. Vermeulen M, van Gijn J. The diagnosis of subarachnoid hemorrhage. J Neurol Neurosurg Psychiatry. 1990; 53:365–72.
17. Edlow JA, Wyer PC. Evidence-based emergency medicine/clinical question: how good is a negative cranial computed tomographic scan result in excluding subarachnoid hemorrhage? Ann Emerg Med. 2000; 36:507–16.
18. Linn FH, Wijdicks EF, van der Graaf Y, Weerdesteyn-van Vliet FA, Bartelds AI, van Gijn J. Prospective study of sentinel headache in aneurysmal subarachnoid haemorrhage. Lancet. 1994; 344:590–3.
19. Wijdicks EF, Kerkhoff H, van Gijn J. Long term follow up of 71 patients with thunderclap headache mimicking subarachnoid hemorrhage. Lancet. 1998; 2:68–70.
20. Markus HS. A prospective follow up of thunderclap headache mimicking subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry. 1991; 4:1117–28.
21. Landtblom AM, Fridriksson S, Boivie J, Hillman J, Johansson G, Johansson I. Sudden onset headache: a prospective study of features, incidence, and causes. Cephalalgia. 2002; 22:354–60.
22. Hirai T, Korogi Y, Ono K, et al. Preoperative evaluation of intracranial aneurysms: usefulness of intraarterial 3D CT angiography and conventional angiography with a combined unit – initial experience. Radiology. 2001; 220:499–505.
23. Matsumoto M, Sato M, Nakano M, et al. Three-dimensional computerized tomography angiography-guided surgery of acutely ruptured cerebral aneurysms. J Neurosurg. 2001; 94:718–27.
24. White PM, Teadsale E, Wardlaw JM, Easton V. What is the most sensitive non-invasive imaging strategy for the diagnosis of intracranial aneurysms? J Neurol Neurosurg Psychiatry. 2001; 71:322–8.
25. Santos N, Machado E, Carvalho S, et al. Subarachnoid hemorrhage and computerized tomography cerebral angiography. Acta Med Port. 2001; 14:43–7.
26. Seruga T, Bune G, Klein GE. Helical high-resolution volume-rendered 3-dimensional computer tomography angiography in the detection of intracranial aneurysms. J Neuroimaging. 2001; 11:280–6.
27. Sidman R, Spitalnic S, Demelis M, Durfey N, Jay G. Xanthchromia? By what method? A comparison of visual and spectrophotometric xanthochromia. Ann Emerg Med. 2005; 46:51–5.
28. Shah KH, Edlow JA. Distinguishing traumatic lumbar puncture from true subarachnoid hemorrhage. J Emerg Med. 2002; 23:67–74.
29. Cloft HJ, Joseph GJ, Dion JE. Risk of cerebral angiography in patients with subarachnoid hemorrhage, cerebral aneurysm, and arteriovenous malformation: a meta-analysis. Stroke. 1999; 30:317–20.
30. Mitchell P, Gholkar A, Vindlacheruvu RR, Mendelow AD. Unruptured intracranial aneurysms: benign curiosity or ticking bomb? Lancet Neurol. 2004; 3: 85–92.
31. Connolly PJ, Biller J, Pritz MB. Aneurysm observation versus intervention: a literature review. Neurol Res. 2002; 24(Suppl 1):S84–95.
32. Brennan JW, Schwartz ML. Unruptured intracranial aneurysms: appraisal of the literature and

suggested recommendations for surgery, using evidence-based medicine criteria. Neurosurgery. 2000; 47:1359–71.
33. Piepgras DG. Clinical decision making in intracranial aneurysms and aneurysmal subarachnoid hemorrhage – science and art. Clin Neurosurg. 1992; 39: 68–75.
34. Johnston SC, Gress DR, Kahn JG. Which unruptured cerebral aneurysms should be treated? A cost-utility analysis. Neurology. 1999; 52:1806–15.
35. U-King-Im JM, Koo B, Trivedi RA, et al. Current diagnostic approaches to subarachnoid hemorrhage. Eur Radiol. 2005; 15:1135–47.
36. Hoh BL, Cheung AC, Rabinov JD, Pryor JC, Carter BS, Ogilvy CS. Results of a prospective protocol of computed tomographic angiography in place of catheter angiography as the only diagnostic and pretreatment planning study for cerebral aneurysms by a combined neurovascular team. Neurosurgery. 2004; 54:1329–42.
37. Asimos AW, Norton HJ, Price MF, Cheek WM. Evaluation of acute contrast-induced nephropathy in acute ischemic stroke patients undergoing routine CT angiography using nonionic contrast [abstract]. Acad Emerg Med. 2004; 11:576.
38. Brenner DJ, Doll R, Goodhead DT, et al. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. Proc Natl Acad Sci U S A. 2003; 100:13761–6.
39. Rinkel GJ, Djibuti M, Algra A, van Gijn J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. Stroke. 1998; 29:251–6.