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REVIEW **DERLEME**

RADIOLOGICAL EVALUATION OF SUBARACHNOID HEMORRHAGE

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ABSTRACT

Nontraumatic subarachnoid hemorrhage is one of the most elusive diagnoses in emergency medicine; it is a potentially lethal disease that is often considered and rarely found. The current practice as determined by the American College of Emergency Physicians 1996 Clinical Policy on Headache is a noncontrast head computed tomography followed by diagnostic lumbar puncture (LP) to exclude subarachnoid hemorrhage. Whereas the guideline does not consider pretest probability of subarachnoid hemorrhage in determining which patients require LP after negative head computed tomography, patients' technical aspects of performing a LP in patients with nonideal anatomy, and risks associated with LP must all be considered when choosing to proceed with invasive testing. The clinical challenges are to determine which patients with acute headache should undergo expensive and invasive diagnostic testing for this both rare and lethal condition and what, if any, low-risk characteristics of the history and physical examination can effectively rule out subarachnoid hemorrhage. As imaging technology such as computed tomography improves, the need for invasive testing with lumbar puncture may decrease. A decision rule to guide clinical practice in low-risk settings would be helpful and should be a focus of further research in this area. his article outlines the use of current testing modalities to provide an up-to-date understanding of diagnostic testing for subarachnoid hemorrhage.
Keywords: Subarachnoid haemorrhage, computed tomography, angiography, diagnosis.

SUBARAKNOİD KANAMANIN RADYOLOJİK OLARAK İNCELENMESİ

ÖZ

Travmatik olmayan subaraknoid kanama, acil tıpta anlaşılması en zor teşhislerden biridir; sıklıkla düşünülen ve nadiren bulunan potansiyel olarak ölümcül bir hastalıktır. Subaraknoid kanamayı dışlamak için American College of Emergency Physicians (Amerikan Acil Doktorlar Koleji) tarafından belirlenen 1996 Baş Ağrısı Klinik Politikası güncel uygulaması: tanısal lomber ponksiyon (LP) ve kontrastsız bilgisayarlı beyin tomografisidir. Kılavuz, negatif bilgisayarlı beyin tomografiden sonra, hangi hastaların LP'ye ihtiyaç duyulduğunu belirlemede subaraknoid kanamanın ön test olasılığını dikkate almazken, ideal anatomiye sahip olmayan hastalarda LP kullanmanın teknik yönleri ve LP kullanımıyla ilgili risklerin tümü, invasif test seçiminde dikkate alınmalıdır. Klinik zorluklar, akut baş ağrısı olan hastaların hangilerinin, bu nadir ve ölümcül durumda, pahalı ve invaziv tanı testlerine tabi tutulması gerektiğini ve eğer varsa hasta geçmişi ve fizik incelemelerinin düşük risk özelliklerinden hangilerinin subaraknoid kanamayı etkili bir biçimde dışlayabileceğini belirlemektir. Bilgisayarlı tomografi gibi görüntüleme teknolojileri geliştikçe, lomber ponksiyon ile invaziv testlere duyulan ihtiyaç azalabilir. Düşük riskli ortamlarda klinik uygulamaya rehberlik etmek için bir karar kuralı yardımcı olacaktır ve bu alandaki daha ileri araştırmanın odağı olmalıdır. Bu makale, subaraknoid kanamanın tanısal testlerin güncel bir şekilde anlaşılmasını sağlamak için mevcut test yöntemlerinin kullanımını özetlemektedir.
Anahtar Sözcükler: Subaraknoid kanama, bilgisayarlı tomografi, anjiyografi, teşhis.

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INTRODUCTION

Nontraumatic subarachnoid haemorrhage (SAH) is a neurological emergency characterised by extravasation of blood into the spaces lining the central nervous system, which are normally filled with liquor. The global incidence of SAH, which varies from region to region, is about 10.5 cases per 100.000 inhabitants per year and has remained stable over the last 30 years. The incidence increases with age, with the mean age of presentation being 55 years. Female-to-male ratio is 1.6:1. Mean mortality of patients with SAH is 51%; one third of survivors require lifelong medical assistance. The main negative prognostic factors include level of consciousness, age and the quantity of blood at initial computed tomography (CT) scan (1,2). The principle variable risk factors are cigarette smoking, hypertension, use of cocaine and alcohol abuse. First-degree family members of patients with SAH have an increased risk; there are also hereditary diseases of the connective tissue associated with intracranial aneurysms and SAH, such as polycystic kidney disease, Ehlers-Danlos syndrome (type IV), pseudoxanthoma elasticum and fibromuscular dysplasia (3).

The importance of early diagnosis and treatment is clear: delayed diagnosis significantly increases mortality and morbidity in SAH. On the basis of these prognostic criteria, an SAH should always be suspected in patients with the typical presentation of sudden and severe headache associated with nausea, vomiting, neck stiffness, photophobia or loss of consciousness. When patients say, "worst headache ever" or "headache unlike any I have had before," the index of suspicion for a serious cause of headache is increased. The physical examination may reveal retinal haemorrhage, evidence of meningeal irritation, reduced level of consciousness and/or focal or unilateral neurological deficit. In the absence of the classic signs and symptoms, SAH can be confused with migraine and tension headaches in 50% of cases (4). Spontaneous SAH is caused by rupture of an intracranial aneurysm in 80%-90% of cases (5). The mortality for untreated aneurysmal SAH is up to 50% in the 1st month, mainly because of rerupture (6). Rapid confirmation or exclusion of the source of a SAH is required to provide optimal patient care.

Digital Subtraction Angiography

Digital subtraction angiography (DSA) has been the main technique to detect and characterize intracranial aneurysms, and carefully performed, remains the gold standard (Figure I). It is nevertheless an invasive procedure and carries a risk of neurological complications of 0.9-2.3% with permanent deficit in 0.3% (7,8). Serious non-neurological complications, which occur in 0.6% of cases, include groin haematoma requiring transfusion or surgical repair, peripheral thromboembolism, transient hypotension and arteriovenous fistulas (9). A sensitive noninvasive diagnostic tool that could be used for acutely ill patients would be a major advantage.

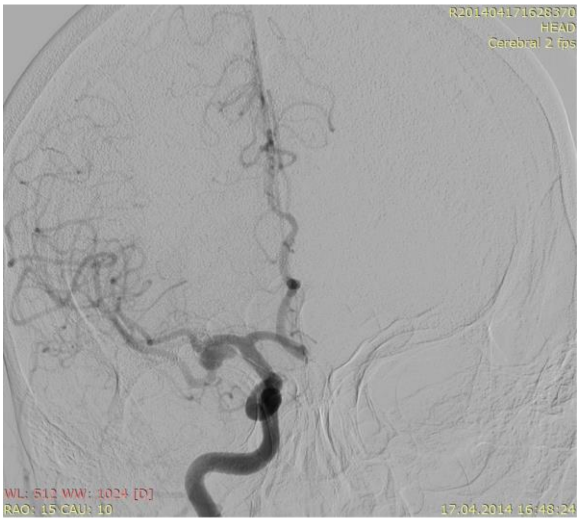

Figure I. Right internal carotid artery anteroposterior selective digital subtraction angiography images. Right middle cerebral artery trifurcation located inferiorly oriented lobulated aneurysmal dilatation.

Unenhanced Computed Tomography

The standard first test, unenhanced cranial CT scan (Figure II), is highly accurate, but like all tests, possesses limitations (10). Firstly, accuracy decays with time; this is due to circulation of cerebrospinal fluid and the resultant dilution and catabolism of the blood. Studies using third-generation scanners demonstrate sensitivities in the range of 90-98% within the first 24 h (11-13). One preliminary report of 913 neurologically intact patients (75 with SAH) with severe, abrupt-onset headaches found CT scan to be 92% sensitive and 100% specific; in the 305 patients scanned within 6 h of headache onset, CT scan was 100% sensitive (95% confidence interval 92–100) (14). By 3 and 7 days after the ictus, the sensitivity falls to 85% and 50%, respectively (15,16). One report using "5th generation" multi-detector CT scanners showed that no SAH case was missed; however, the study was underpowered, which yielded a lower 95% confidence interval of only 61% (17). The second important limitation of CT is "spectrum bias." In alert and awake patients (presumably with smaller volume bleeds), the scans are less likely to show blood. These first two limitations- reduced accuracy over time and spectrum bias—are extremely important for emergency physicians to understand. Thirdly, intracranial blood in anemic patients (hematocrit < 30%) may appear isodense with brain and thus be more difficult to see (18). Lastly, many of these CT sensitivity studies relied on experienced neuroradiologists' interpretations, and "real world" readings by general radiologists, neurologists, or emergency physicians are less accurate (19). False-positive CT scans for SAH are unusual but have been reported in the settings of intravenous contrast neurotoxicity, purulent meningitis, spontaneous intracranial hypotension, isodense subdural hematomas, confusion with normal dural structures, and diffuse cerebral edema (20). Whenever meningitis is a strong possibility, intravenous antibiotics should be administered rapidly.

Lumbar Puncture

In patients where CT is negative or equivocal after evaluation by an experienced clinician or radiologist, the next stage in making the diagnosis should be to perform a lumbar puncture. This procedure should be carried out as a planned procedure by a suitably experienced clinician as a single atraumatic puncture is essential to avoid a ''bloody tap''. A primary drawback to the CT-LP approach is the complication rate of LP. A study of 376 patients who underwent LP for the evaluation of SAH revealed the following frequency of complications: backache (37%), headache (34%), severe radicular pain (15%), and paraparesis (1.5%). Paraparesis due to spinal hematoma occurred only in patients who were given anticoagulants within 1 hour after the procedure, or who were concurrently taking aspirin (21). A review of clinical trials evaluating bedrest in the prevention of post-LP headaches quoted a 33% incidence of post-LP headaches (22). Another drawback of LP is the diagnostic uncertainty created by the high rate of local trauma from the spinal needle, which can introduce peripheral blood into the cerebrospinal fluid (CSF) sample (ie, a traumatic tap). Rates of traumatic tap have been reported at 10% in a recent study of 1489 bedside procedures in an academic teaching hospital (23).

Figure II. Axial unenhanced computed tomography. Increased density secondary to the bleeding of aneurysmal dilatation localized at the left middle cerebral artery trifurcation.

Computed Tomographic Angiography

Early studies of computed tomographic angiography (CTA) both for general vascular and neurovascular indications showed significant promise as a result of this advance (24). The growing clinical applications of CTA in the past decade can be attributed to the development of helical multidetector row CT (MDCT) scanners with increasing numbers of detector rows, which enable the acquisition of CTA with greatly increased speed and quality. However, because of the increase in the number of image slices per study and the difficulty of depicting the complex neurovascular tree with multidetector CTA (MDCTA), three dimensional (3D) postprocessing has become increasingly important for the interpretation of MDCTA examinations.

The shift in management of ruptured intracranial aneurysms from surgery to endovascular means, initially with detachable balloons, and in the early 1990s with Guglielmi electrolytically detachable coils, has increased pressure on angiographic resources in many centers. This has been further exacerbated by the results of the International Subarachnoid Aneurysm Trial which showed a relative and absolute risk reduction in death or dependency of 22.6 and 6.9%, respectively, in coiled versus clipped patients with acute SAH (25-27). As a result of this, coil treatment is now the mainstay of securing ruptured aneurysms in many European centres (28,29). Besides identification of aneurysms, CTA may provide additional useful information on the topography of the aneurysm (Figure III). The limiting factors for CTA remain mainly a limited spatial resolution and lack of information on flow dynamics (30). CTA has been applied to the detection of ruptured and unruptured intra-cranial aneurysms for several years.

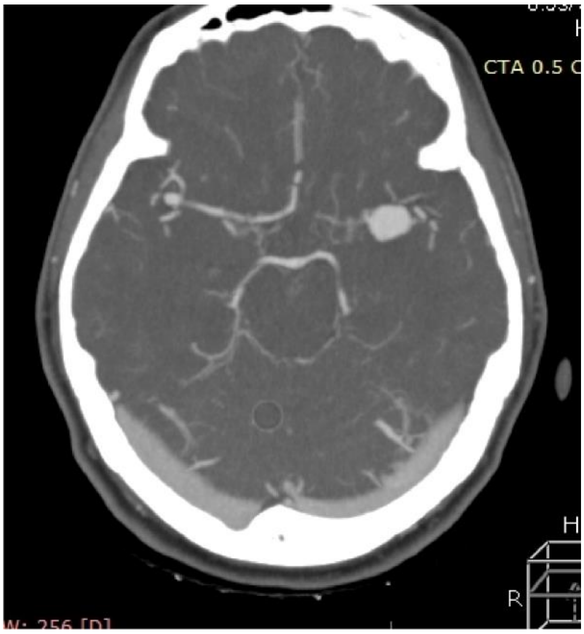

Figure III. Contrast-enhanced axial computed tomography angiography examination. Two lobulated aneurysms located bilateral middle cerebral artery trifurcations.

Systematic Reviews: Table I summarizes the meta-analyses of CTA for detection of cerebral aneurysms. The systematic review of studies performed with single - detector row CTA conducted by White et al. demonstrated a sensitivity of 90% and a specificity of 86% in the detection of aneurysms when compared with DSA (24). Magnetic resonance angiography (MRA) had a similar accuracy to CTA of 89-90% with a higher specificity of 95% (versus 86%) and a slightly lower sensitivity of 87% (versus 90%). However, the sensitivity of MRA fell dramatically to 38% for aneurysms 3 mm or smaller whereas the sensitivity for CTA for these aneurysms remained 61%. A more recent meta-analysis by Chappell et al. showed CTA to have sensitivity 92.7% and a specificity of 77.2% when the studies were weighted for the number of patients in each study (31). Van Gelder undertook a further analysis of CTA accuracy in detecting and excluding aneurysms with the majority of studies performed between 1993 and 1998 (therefore single-section). CTA sensitivity ranged from 53% for aneurysms 2 mm in size to 95% for 7 mm aneurysms. Overall specificity was 98.9% (32). In their studies, the prevalence of aneurysms was high, which is reflected in the favorable sensitivity for larger aneurysms. The sensitivity for small aneurysms was not consistent, but the overall low sensitivity may reflect the technology used. One can appreciate the link between the aneurysm prevalence in the studies and the reported sensitivity of CTA.

Blinded Studies (Single Section): Table II summarizes the main comparative, blinded CTA studies. A large study by White et al. in 2001 (included in the van Gelder meta-analysis) reported a low sensitivity of 68%.(33) Low aneurysm prevalence, empirical fixed delay between contrast infusion and imaging, use of non-spiral CT in a small number of patients (20 of 162 cases) and use of standard reformatted projections using bone editing may have contributed to this. Villablanca et al. showed sensitivity for very small aneurysms was 98–100% for CTA and 95% for DSA when correlated with surgical findings.(34) The same author demonstrated equivalent sensitivity of 97% for CTA and DSA for detection of middle cerebral artery aneurysms.(35) Both studies demonstrated 100% specificity. However, this is an experienced center, the studies focused on detection of small aneurysms, and patients were selected on the basis of a very high probability of harbouring an aneurysm (high

Table I. Meta-analyses of single-section computed tomography angiography studies.

Author	Number of patients	Publication year of studies	Sensitivity/specificity per aneurysm	Sensitivity by size (mm)
White et al.[20] (2000)	677	1988-1998	90/86	≤3: 61%, 3–10: 93%, >10: 100%
Van Gelder et al.[22] (2003)	619	1994-2001	83.6/98.9	2: 53%, 3: 67%, 5: 87%, 7: 95%
Chappell et al.[21] (2003)	1197	1995-2002	92.7/77.2	-

Table II. Blinded studies.

Author	Number of patients	Prevalence of aneurysm	Sensitivity/specificiy per aneurysm	Sensitivity by size
Seruga et al.[28] (2001)	142	90	93.8/100	≤3: 71%, >3: 100%
White et al.[23] (2001)	162	44	68/76	<3: 40%, 3–5: 61%, 5–10: 92%, >10: 100%
Villablanca[24] (2002)	70	49	99/100	≤3: 96%, >3: 100%
Karamessini et al.[26] (2004)	70	64.3	88.7/100	<3: 60%, 3–4: 83%, >4: 100%
Wintermark et al.[30] (2003)	50	80	94.8/94.9	<2: 50%, 2–3: 89%, 3–4: 94%, >4: 100%
Dammert et al.[31] (2004)	50	82	89.5/83.3	<4: 83%, 5–12: 91%, >13: 100%
Jayaranam[32] (2004)	35	60	85.5/93	-

prevalence). They also used multiple reconstruction algorithms to optimize aneurysm detection. Karamessini et al. and Kato et al. found almost identical sensitivities for DSA and CTA for cerebral aneurysms (36,37). Overall sensitivity in several studies for small aneurysms (3-4 mm) ranged from 60-96% (34,36,38). Hope et al. conducted a blinded study comparing limited volume single-section CTA (using three dimensional reconstructions) with DSA in 80 patients (included in the meta-analysis by White et al.) (35). There were 14 of 19 false-positive and nine of 94 false-negative examinations in their study. This was a well-conducted study but is of historical interest as thinner sections are now used (a significant factor in their results), earlier arterial phase imaging is employed (the duration of their study protocol was 40 s), and they relied on reconstructed images alone for analysis. Hashimoto et al. performed CTA in patients with an aneurysmal pattern of SAH who had negative standard DSA (39). He found six aneurysms in 15 patients: Five at the anterior communicating artery junction and one at the middle cerebral artery bifurcation. CTA should therefore be considered as an early second-line investigation in this situation, particularly if three-dimensional rotational angiography (3DRA) is not available (39).

Blinded Studies (Multi-section): Several blinded studies have been reported comparing multisection CTA with DSA for detection of aneurysms, although with relatively small numbers. Wintermark et al. had favorable results with overall sensitivity and specificity approaching 95%: 50% for aneurysms <2 mm; 89-94% 2-4 mm and 100% >4 mm (40). Dammert et al. reported a study involving three trained neuroradiologists, blinded to clinical and angiographic data, who reviewed the CT angiograms of 50 consecutive patients presenting with intra-cranial hemorrhage considered to be aneurysmal (41). Jayaraman et al. reported an average sensitivity of 85.5% which is at the lower end of the sensitivity of the meta-analyses of single section CT (83.6–93.7%) (42). However, the authors had little experience in interpreting CTA and the number of patients included in the study was low. An important factor influencing the accuracy of CTA for the detection and depiction of intracranial aneurysms is the experience and the (perceptual) accuracy of the observer. Pedersen et al. reported an increase in sensitivity from 88% to 94% after 1 year of observer experience (43). White et al. compared the sensitivity and specificity of CTA for the detection of cerebral aneurysms between neuroradiologists and non-neuroradiologists and found neuroradiologists to perform consistently better than the other observers (44). Several studies that used four-detector row spiral machines restricted the area of coverage to the proximal circle of Willis and missed distal pericallosal and posterior inferior cerebellar aneurysms (45). Perianeurysmal blood and the presence of intra-aneurysmal thrombus may reduce lesion conspicuity (46). Surrounding arteries and fenestration of arteries may also obscure the presence of an aneurysm (47). Furthermore, suboptimal arterial enhancement and artifacts caused by patient movement may limit the depiction of aneurysms (48). Vascular infundibula of the posterior communicating or anterior choroidal artery origins may be mistaken for aneurysms if a vessel cannot be identified arising from them (49). Tight vascular loops may also masquerade as aneurysms. Furthermore, small aneurysms may carry a higher risk of being false-positive (50,51).

Magnetic Resonance Imaging

A single study of 22 patients with SAH demonstrated 100% sensitivity of MRI with fluid-attenuated inversion recovery (FLAIR) sequence imaging as compared with 91% sensitivity of CT in acute SAH and 100% sensitivity of gradient echo T2-weighted images vs. 45% sensitivity of CT in subacute/chronic SAH (52). A separate study of MRI in CT negative and LP positive SAH failed to show an advantage over LP with FLAIR sequence imaging alone, but did not stratify patients based on event-to-imaging time (53). A third study showed gradient echo T2-weighted and FLAIR images to be 94% and 81% sensitive in the acute phase and 100% and 87% sensitive in the subacute phase, respectively (54). Unfortunately all of these studies are underpowered, explaining in part the variations in reported sensitivities of FLAIR sequence imaging. There are other advantages of MRI to consider, such as the ability to concurrently detect cerebral aneurysms with magnetic resonance angiography as opposed to pursuing CT angiography. MRI also has the advantage of broadening the scope of diagnostic evaluation (detection of brain tumors, meningial enhancement, cerebral venous thrombosis, and parenchymal abnormalities not well evaluated by CT). The primary limitations of MRI are the time required to perform studies (although examination times have decreased as stronger magnets are being introduced), contraindications in patients with magnetic-susceptible implanted hardware and/or patient size considerations, and the relative difficulty of obtaining MRIs in emergency departments.

Rendering Technique: Maximum Intensity Projection (MIP)

Rendering techniques convert information from the three-dimensional dataset into a two-dimensional image that can be viewed in any plane. MIP pixel value is determined by the maximum X-ray attenuation in the review plane (55). High-density structures (e.g., skull base, calcification) will obscure detail provided by vascular contrast material. Additionally, vessels that cross or overlap each other are not displayed as higher density. Therefore there is a limited appreciation of the spatial relationship of vascular structures in three dimensions. A further potential drawback is increased background noise compared with MPRs (55). An MIP thickness of 2.5 mm is usually sufficient to minimize partial volume averaging and maximize contrast between vessels and brain. For detailed information on a specific feature of an aneurysm (e.g., locating the exact origin of vessels, demonstration of the neck) MIP and volume rendering (VR) are complementary.

Volume Rendering Technique

VR uses the full dataset to reconstruct the image (Figure IV). The pixel values are a combination of attenuation values through the imaging volume, and opacity setting of the software program which weights the voxel value according its position relative to the viewer (55). High opacity will tend to show the surface contour of an aneurysm and low opacity will allow internal architecture to be appreciated. VR images are less useful than MIP and MPR for demonstrating the presence and anatomy of small aneurysms but provide a good overview of aneurysm morphology, particularly in areas of complex anatomy, difficult to review in two dimensions (e.g. middle cerebral artery bifurcation, posterior inferior cerebellar artery (PICA) origin (35). However, predictable artefacts may be seen. VR may incorporate vessels into the reconstruction if they cross or make contact with an area of interest, which may have a significant impact on patient management. Small vessels may not be visualized and cannot be restored by image manipulation in these formats. VR may also cause artefactual broadening of the aneurysm neck, also potentially influencing treatment method.

Surface Rendering (Shaded Surface Display)

Shaded surface display (SSD) reconstructions often produce impressive images but almost never provide significant additional information. The appearance of the images can vary dramatically with differing segmentation thresholds, e.g., vessels can appear stenotic (simulating vasospasm or atheroma). The grey (or colour) scale of SSD images is mainly a simulation of light reflection not

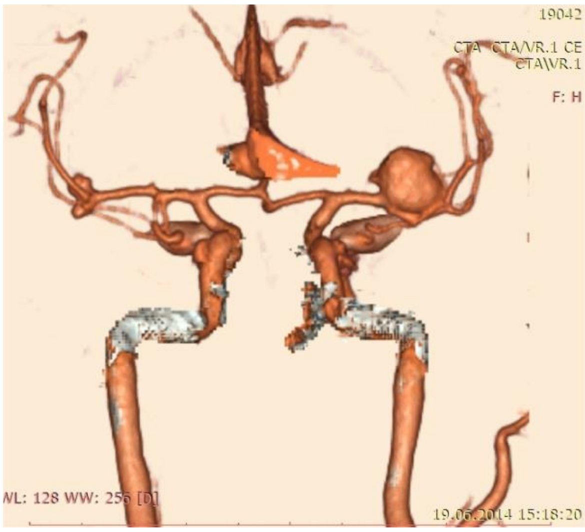

Figure IV. Coronal volume rendering technique image. Two lobulated aneurysms located bilateral middle cerebral artery trifurcations.

a representation of differing X-ray attenuation, and obscuration of important vascular detail is inevitable. It is difficult to select a threshold that will differentiate bone from vascular contrast causing these structures to merge with one another. These reconstructions are usually supplementary to MIP and MPR images. This review process is initially time-consuming taking between 30-45 min. With experience a detailed analysis can be performed in 10-15 min, which is significantly shorter than the time taken to perform and interpret a cerebral angiographic study (45). Having a strategy for reviewing systematically the primary branching points of the Circle of Willis will reduce the chances of missing small ruptured aneurysms and coincidental lesions. CTA, however, provides no information on the aortic arch, anatomic variations of the major vessel origins, the presence of vascular stenosis or sub-cranial vascular loops. All of these may compromise the success of endovascular treatment.

CONCLUSIONS

In emergency medicine practice, nontraumatic SAH is a diagnosis that is often suspected and infrequently encountered when pretest probability is low. It is even rarer when a noncontrast head CT is negative. The clinical challenges are to determine which patients with acute headache should undergo expensive and invasive diagnostic testing for this both rare and lethal condition and what, if any, low-risk characteristics of the history and physical examination can effectively rule out SAH. As imaging technology such as CT improves, the need for invasive testing with lumbar puncture may decrease. A decision rule to guide clinical practice in low-risk settings would be helpful and should be a focus of further research in this area.

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Ethics
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Authorship Contributions: Surgical and Medical Practices: EC, NB, CS, Concept: EC, NB, CS, Design: EC, NB, CS, Data Collection or Processing: EC, NB, CS, Analysis or Interpretation: EC, NB, CS, Literature Search: EC, NB, CS, Writing: EC, NB, CS.
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