Detection of Subarachnoid Hemorrhage at Acute and Subacute/Chronic Stages: Comparison of Four Magnetic Resonance Imaging Pulse Sequences and Computed Tomography

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Background: Acute subarachnoid hemorrhage (SAH) has traditionally been diagnosed by computed tomography (CT); however, fluid-attenuated inversion recovery (FLAIR) is a magnetic resonance imaging (MRI) modality currently used to detect acute SAH. CT is insensitive in the detection of subacute or chronic SAH. The purpose of this study was to compare 4 MRI pulse sequences and CT in the detection of SAH in acute and subacute-to-chronic stages.

Methods: From 2001–2003, we collected data for 22 patients (12 men and 10 women, aged 35–80 years) with SAH due to ruptured aneurysm (n = 11), trauma (3), or unknown origin (8). All patients underwent MRI and CT examination, with an interval of less than 12 hours between the 2 procedures. We divided patients into 2 groups according to the time from symptom onset to MRI evaluation: patients with MRI performed ≤ 5 days post-ictus had acute-stage illness, whereas patients with MRI performed from day 6–30 post-ictus had a subacute-to-chronic condition. MRI (1.5-T) pulse sequences comprised spin-echo T1-weighted, fast spin-echo T2-weighted, FLAIR, and gradient-echo (GE) T2*-weighted images.

Results: In the acute-stage group, SAH was seen as an area of high signal intensity compared with surrounding cerebrospinal fluid in 36.4% of cases on T1-weighted images, and in 100% on FLAIR images; low signal intensities were seen in 18.2% of cases on T2-weighted images, and in 90.9% on GE T2*-weighted images. High-attenuated SAH was seen on CT in 90.9% of cases. FLAIR (p = 0.008), GE T2*-weighted images (p = 0.012) and CT images (p = 0.012) were all statistically significant indicators of acute SAH. In the subacute/chronic-stage group, SAH was detected on T1-weighted images (36.4% of cases), FLAIR (33.3%), T2-weighted images (9.1%), GE T2*-weighted images (100%), and CT (45.5%). GE T2*-weighted images were significantly superior (p = 0.001) to other MRI pulse sequences and CT as indicators of subacute-to-chronic SAH.

Conclusion: FLAIR and GE T2* MRI pulse sequences, and CT scans, are all statistically significant indicators of acute SAH. GE T2*-weighted images are statistically significant indicators of subacute-to-chronic SAH, whereas other MRI pulse sequences, and CT scans, are not. [*J Chin Med Assoc* 2005;68(3):131–137]

Key Words: computed tomography, magnetic resonance imaging, subarachnoid hemorrhage

Introduction

Computed tomography (CT) has high sensitivity for detecting acute subarachnoid hemorrhage (SAH), and also has short scan times and widespread availability. Thus, since its introduction into clinical practice, CT has been the imaging investigation of choice in cases of suspected SAH. Lumbar puncture is performed in

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cases of highly suspected SAH with negative CT findings. The sensitivity of CT for detecting SAH is more than 90% within a day of hemorrhage, but falls off rapidly over time and approaches 0% at 3 weeks, especially in cases where the bleed is small.[1] Conventional magnetic resonance T1- and T2-weighted images are relatively insensitive indicators of SAH. Scan times for magnetic resonance imaging (MRI) are longer than those for CT, and MRI restricts patients more than CT, making it unsuitable for confused or restless patients. In 1994, Noguchi et al[2] first reported the use of a fluid-attenuated inversion recovery (FLAIR) MRI sequence for the detection of acute SAH in 3 cases, and there has been general agreement that the sensitivity of MRI for detecting SAH increases over the few days after a bleed.[3] As this is when the sensitivity of CT falls, MRI would be expected to have greater sensitivity than CT after a time interval from the hemorrhage. The use of a gradient-echo (GE) T2*-weighted MRI sequence to detect subacute SAH was first reported in 2001 by Mitchell et al.[1]

The purpose of the current study was to evaluate the detection rate of the 4 abovementioned MRI sequences and CT in patients with acute or subacute-to-chronic SAH.

Methods

Patient population

The study group comprised 22 patients (12 men and 10 women, aged 35–80 years) with SAH due to ruptured aneurysm (n = 11), trauma (3), or unknown origin (8). Because the sensitivity of MRI and CT depends on time from the clinical hemorrhagic event, we divided the series into 2 groups: an acute group, who underwent MRI within 5 days of ictus; and a subacute/chronic group, who underwent MRI within 6–30 days of ictus. All patients, or their relatives, gave informed consent for the procedures.

CT and MRI scan protocols

All patients underwent CT up to 12 hours before MRI study. Non-contrast CT was performed with a 4-mm slice thickness in the posterior fossa, and with an 8-mm slice thickness in other brain regions. MRI scans were performed with a 1.5-T system and comprised the following sequences: axial T1-weighted spin-echo (433/14/2 [repetition time, echo time, excitations]); T2-weighted fast spin-echo (4000/100/2) with echo train length 8; fast FLAIR (9002/2200/133/1 [repetition time, inversion time, echo time, number of excitations]); and GE T2*-weighted (567/20/25 [repetition time, echo time, flip angle]). Sections 5 mm thick, with 2.5-mm interslice gaps, 24-cm field of view, and 256 × 192 matrix, were used for all scans. FLAIR images were only available for 14 of the 22 patients, whereas the other 3 MRI pulse sequences were performed in all patients.

Image interpretation

The MRI and CT scans were assessed independently by 3 experienced neuroradiologists. All judgments were made by consensus of the 3 reviewers. SAH was clearly demonstrated as a high signal-intensity area, compared with normal cerebrospinal fluid (CSF), on T1-weighted and FLAIR images (FLAIR images suppress the normal hyperintensity of CSF), and as a low signal-intensity area on T2-weighted and GE T2*-weighted images. The detection rate of SAH was evaluated by CSF examination via lumbar puncture (n = 11), surgical findings (7), or both (6). The presence or absence of SAH was recorded on all scans in the following areas: the cortical sulci and sylvian fissures; the ventricular system, and subarachnoid cisterns. Specific SAH detection rates were calculated as the number of SAH cases identified by each of the 4 different MRI sequences, or CT, divided by the total number of SAH cases in each patient group.

Statistical analysis

Statistical analysis of SAH detection rates was conducted using a binomial test, with the test proportion set to 0.5 (50%). A p value of less than 0.05 was considered statistically significant. The analysis was conducted using Statistical Package for the Social Sciences version 10.0 for Windows (SPSS Inc, Chicago, IL, USA).

Results

In the acute-stage group (MRI performed ≤ 5 days post-ictus), SAH was seen as an area of high signal intensity in 4 of 11 patients on T1-weighted images (detection rate, 36.4%; not significant [ns]), and in 8 of 8 patients on FLAIR images (100%; p = 0.008); SAH was seen as an area of low signal intensity in 2 of 11 patients on T2-weighted images (detection rate, 18.2%; ns), and in 10 of 11 patients on GE T2*-weighted images (90.9%; p = 0.012). High-attenuation SAH was seen on CT scan in 10 of 11 patients (detection rate, 90.9%; p = 0.012; Figures 1 and 2). Thus, FLAIR and GE T2*-weighted MRI pulse sequences, and CT scan, were all statistically significant indicators of acute SAH.

In the subacute/chronic-stage group (MRI performed within 6–30 days of ictus), SAH was detected in 4 of 11 patients on T1-weighted images (detection rate, 36.4%; ns), 2 of 6 patients on FLAIR images (33.3%; ns), 1 of 11 patients on T2-weighted images (9.1%; ns), and in all 11 patients on GE T2*-weighted images (100%; $p = 0.001$). High-attenuation SAH was seen on CT scan in 5 of 11 patients (detection rate, 45.5%; ns; Figure 3). Thus, GE T2*-weighted images were statistically significant indicators of subacute-to-chronic SAH, whereas other MRI pulse sequences, and CT scans, were not. Figure 4 shows SAH detection rates for each scanning procedure, expressed as the percentage of patients with SAH shown by the procedure, divided by the total number of patients with SAH confirmed by lumbar puncture and/or surgical findings.

Discussion

The pathophysiology of SAH and the physical principles of CT explain the changes that occur, over time from ictus, regarding the sensitivity of CT for detecting SAH. X-ray techniques, including CT, produce tissue contrast because some of the X-ray beam is stopped (attenuated) by the tissue. This depends on 2 factors: the amount of tissue traversed by the beam, and the

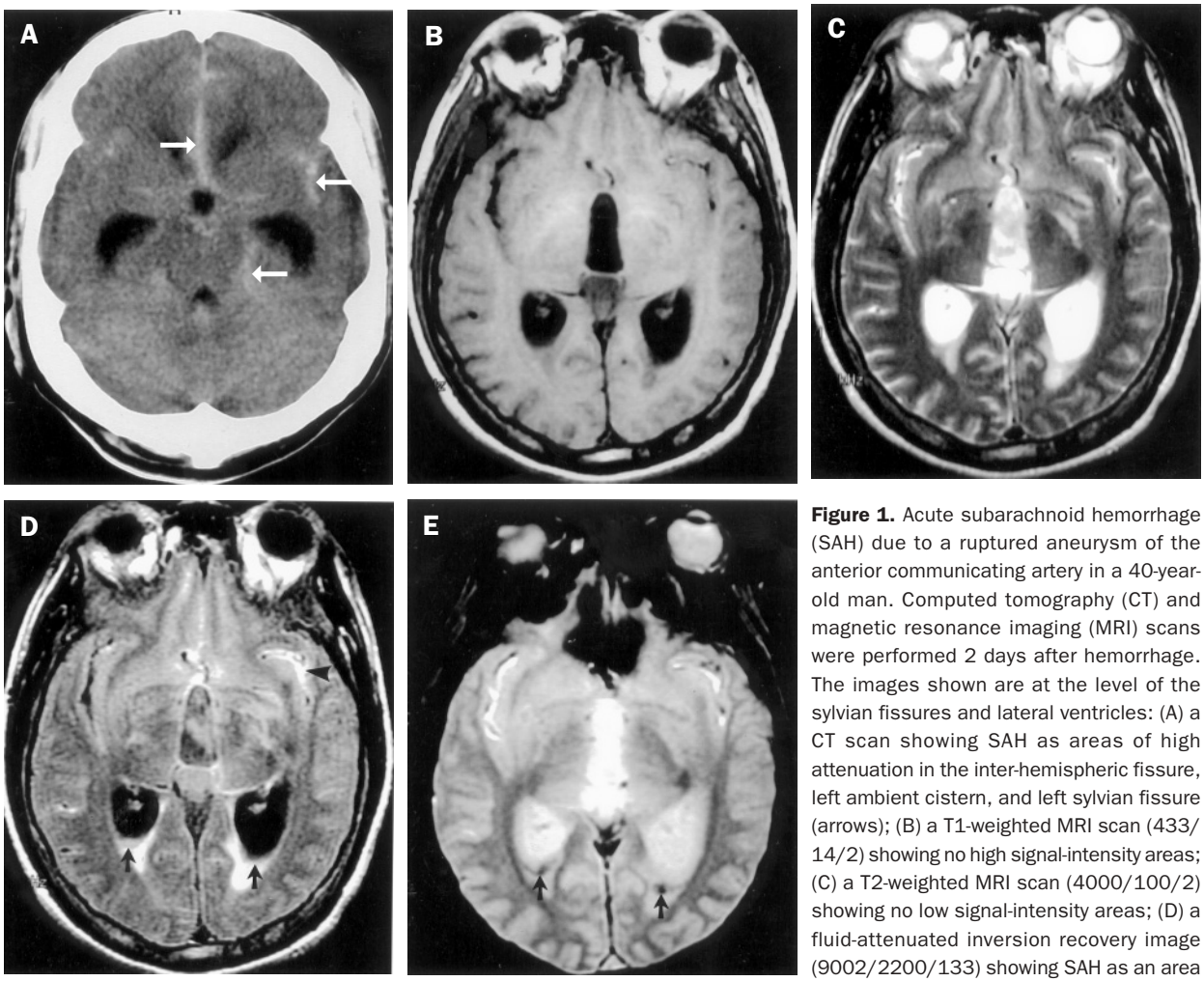

Figure 1. Acute subarachnoid hemorrhage (SAH) due to a ruptured aneurysm of the anterior communicating artery in a 40-year-old man. Computed tomography (CT) and magnetic resonance imaging (MRI) scans were performed 2 days after hemorrhage. The images shown are at the level of the sylvian fissures and lateral ventricles: (A) a CT scan showing SAH as areas of high attenuation in the inter-hemispheric fissure, left ambient cistern, and left sylvian fissure (arrows); (B) a T1-weighted MRI scan (433/14/2) showing no high signal-intensity areas; (C) a T2-weighted MRI scan (4000/100/2) showing no low signal-intensity areas; (D) a fluid-attenuated inversion recovery image (9002/2200/133) showing SAH as an area of high signal intensity in the left sylvian fissure (arrowhead), and blood in bilateral occipital horns of the lateral ventricles (arrows); (E) a gradient-echo T2*-weighted image (567/20/25) showing blood as a low signal-intensity area in bilateral occipital horns of the lateral ventricles (arrows).

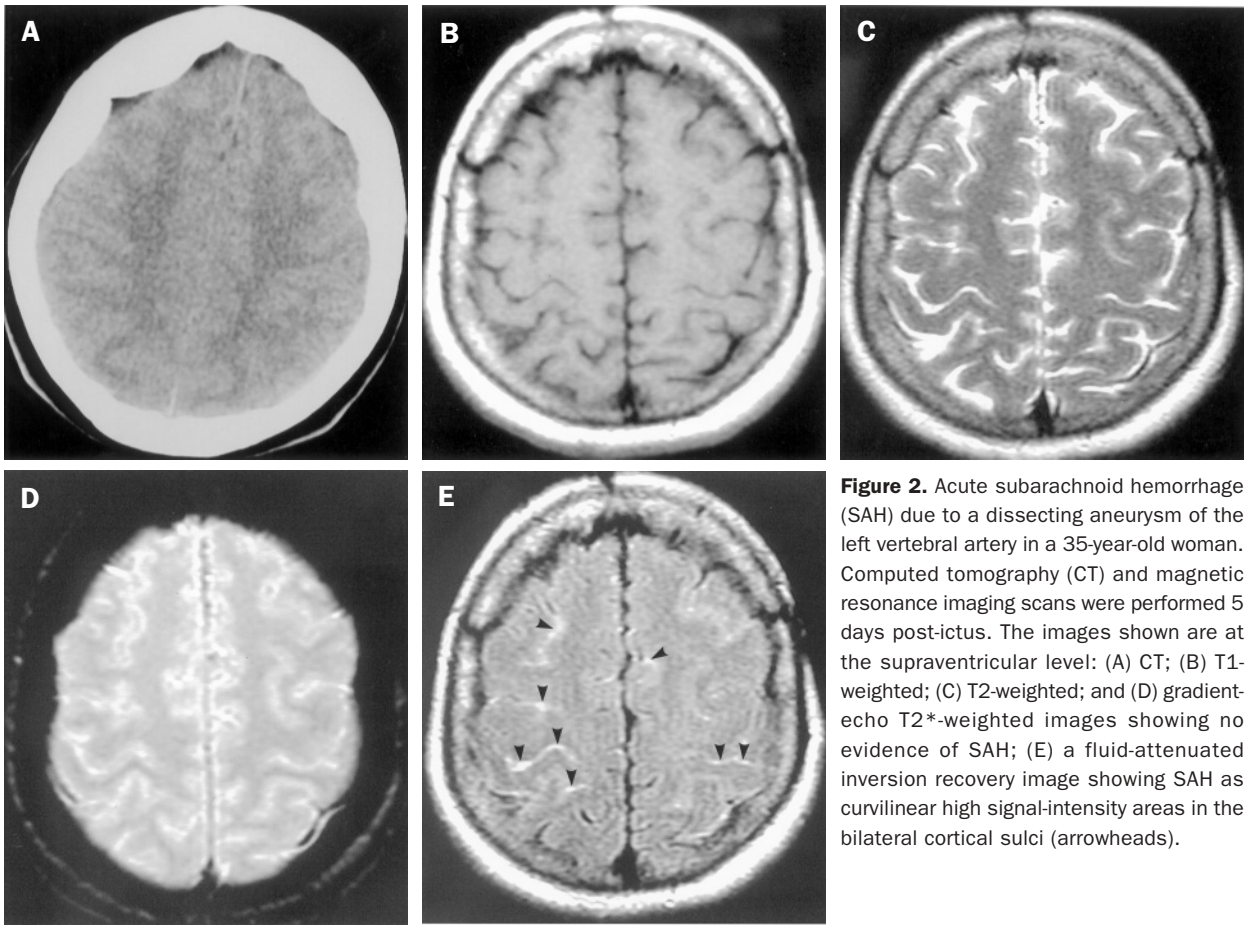

Figure 2. Acute subarachnoid hemorrhage (SAH) due to a dissecting aneurysm of the left vertebral artery in a 35-year-old woman. Computed tomography (CT) and magnetic resonance imaging scans were performed 5 days post-ictus. The images shown are at the supraventricular level: (A) CT; (B) T1-weighted; (C) T2-weighted; and (D) gradient-echo T2*-weighted images showing no evidence of SAH; (E) a fluid-attenuated inversion recovery image showing SAH as curvilinear high signal-intensity areas in the bilateral cortical sulci (arrowheads).

attenuation coefficient of the tissue. Fresh hemorrhage has the same electron density as brain and other soft tissue, and so hyperacute (within 2 hours of ictus) SAH may not be seen directly on CT. As reabsorption of serum from hematoma progresses, local packed cell volume and, hence, electron density increase, making acute SAH visible as a high-attenuated "white" area. With the passage of further time, SAH becomes less visible on CT, principally because of 2 processes. First, CSF circulation redistributes focal SAH into other parts of the subarachnoid space and ventricular systems. The resulting dilution reduces conspicuity on CT. Second, reabsorption of serum is followed by reabsorption of protein, which also leads to reduced conspicuity. Consequently, the sensitivity of CT to SAH falls dramatically over the first 14 days from ictus.

MRI, however, does not rely directly on the electron density of substance for its contrast resolution. The MRI signal relies principally on proton (hydrogen nuclei) density, and T1 and T2* (which includes the T2 component) relaxation times. Moreover, SAH on MRI does not follow the T1 and T2 characteristics of other intracranial hemorrhage, but depends mainly on differences in T1 and T2 relaxation times between SAH and the surrounding CSF and brain parenchyma.[1] Interestingly, based on their *in vitro* data for CSF-to-blood ratios, especially low ratios, Chakeres and Bryan[4] postulated that MRI might be superior to CT for detecting SAH.

The 2 primary mechanisms for T1 shortening in hemorrhage are bound-water effects and paramagnetic effects.[5–7] There is little formation of methemoglobin until several days after SAH, but immediately after SAH, there is a small decrease in T1 relaxation time, reflecting an increase in hydration-layer water due to an increased protein content in bloody CSF.[8] The latter factor also leads to a subtle increase in signal intensity in the CSF on T1-weighted images. Several days after ictus, an increase in signal intensity in the subarachnoid spaces is due to significant methemoglobin formation. However, in mild SAH, red blood cells (RBCs) may be reabsorbed by this time, such that significant methemoglobin formation would not occur, and the anticipated short T1 appearance would not be seen.[6,8]

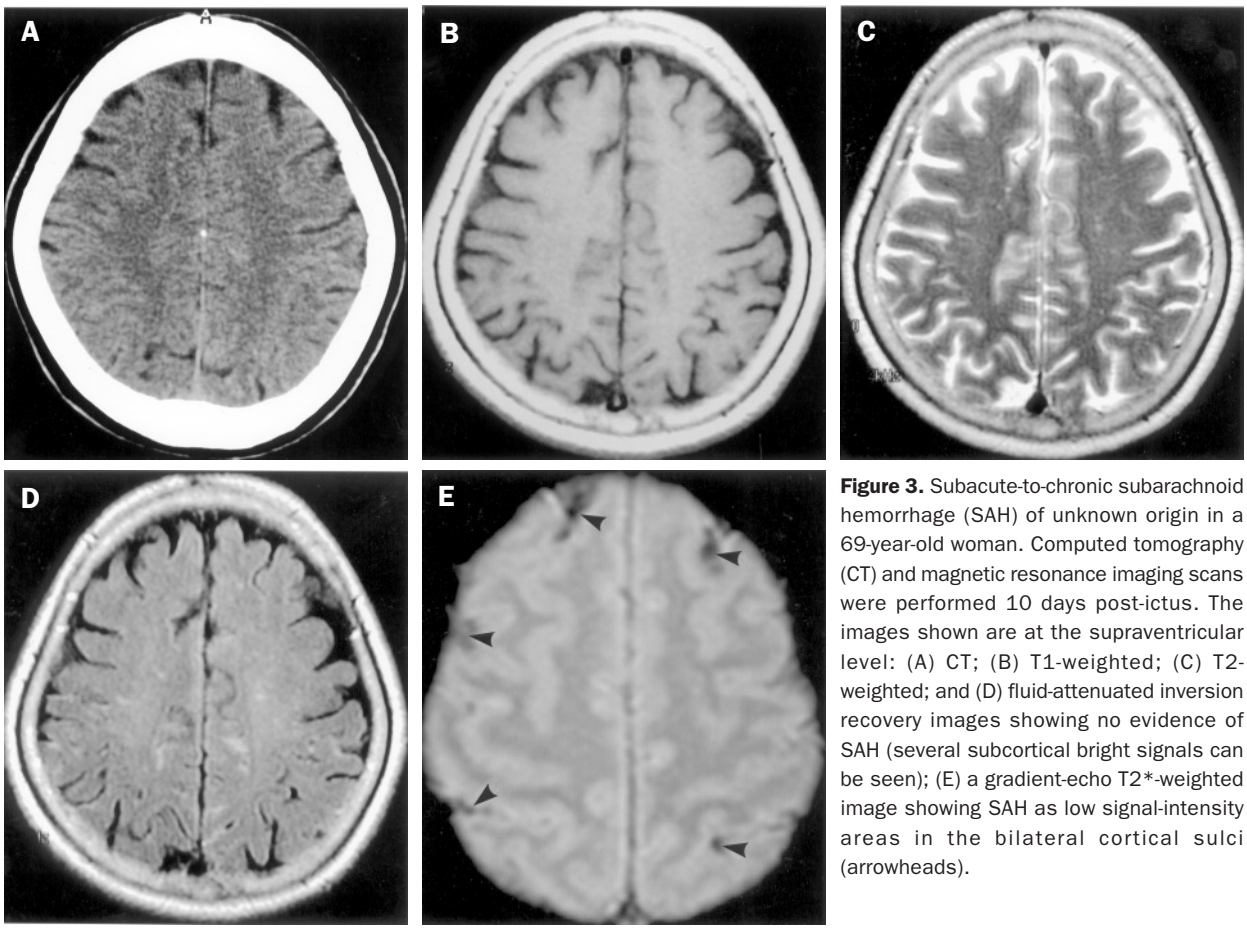

Figure 3. Subacute-to-chronic subarachnoid hemorrhage (SAH) of unknown origin in a 69-year-old woman. Computed tomography (CT) and magnetic resonance imaging scans were performed 10 days post-ictus. The images shown are at the supraventricular level: (A) CT; (B) T1-weighted; (C) T2-weighted; and (D) fluid-attenuated inversion recovery images showing no evidence of SAH (several subcortical bright signals can be seen); (E) a gradient-echo T2*-weighted image showing SAH as low signal-intensity areas in the bilateral cortical sulci (arrowheads).

A characteristic, marked T2 shortening due to deoxyhemoglobin is observed in acute intraparenchymal hemorrhage.[9] However, SAH differs from intraparenchymal hemorrhage because it is mixed with CSF at high oxygen tension. Grossman et al[10,11] presented *in vitro* data suggesting that such high oxygen tension of CSF restricts the generation of paramagnetic deoxyhemoglobin in CSF blood; they also proposed that CSF blood is not seen as an area of marked hypointensity on T2-weighted images because of low hematocrit and a lack of deoxyhemoglobin formation from diamagnetic oxyhemoglobin. Hayman et al[12] postulated that signal intensity on T2-weighted images depends primarily on RBC hydration status, and that RBC dehydration causes the T2 relaxation time to markedly decrease relative to that of brain parenchyma, whereas RBC overhydration or lysis causes a marked increase. Therefore, the lack of marked hypointensity on T2-weighted images in SAH may be due to low hematocrit and RBC overhydration and lysis, rather than dehydration, because of bleeding into the CSF space under high oxygen tension and limited generation of paramagnetic deoxyhemoglobin.

The abovementioned mechanisms may explain the unsatisfactory rate of SAH detection using conventional

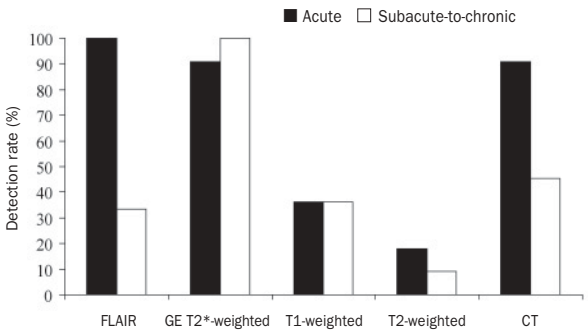

Figure 4. Detection rates of acute and subacute-to-chronic subarachnoid hemorrhage (SAH) for 4 magnetic resonance imaging pulse sequences and computed tomography (CT); for each scanning procedure, the detection rate is expressed as the percentage of patients with SAH identified by the procedure, divided by the total number of patients with SAH confirmed by lumbar puncture and/or surgical findings. FLAIR = fluid-attenuated inversion recovery; GE = gradient-echo.

T1-weighted and T2-weighted MRI scans in our study and previous reports. However, it was previously demonstrated that acute SAH diluted by CSF that is not well visualized as a high-attenuation area on CT sometimes appears as a high signal-intensity area on FLAIR MRI scans.[13] MRI versus CT offers 2 possibilities for the improved detection of SAH, both of which depend on the appearance of hemoglobin and its breakdown products. The protein component of hemorrhage produces high signal, which is swamped by the bright T2 signal from CSF on a conventional T2-weighted image. FLAIR images, because of their long echo time, suppress the normally high CSF signal and produce heavily T2-weighted effects, thus allowing signals from hemoglobin and its breakdown products to be seen.[1] However, artifacts due to CSF pulsation with fast FLAIR imaging have been described.[13–15]

FLAIR imaging was also particularly useful for demonstrating small areas of SAH in the sylvian fissures and cerebral sulci that were difficult to evaluate with conventional MRI and CT, since CSF inflow artifacts may not be seen in these brain regions.[14,15] Our study also indicates that FLAIR images can detect small amounts of SAH in the cortical sulci that are not visible on CT (Figure 2).

Although FLAIR was superior to GE T2*-weighted images and CT for detecting acute SAH (≤ 5 days post-ictus) in our study, all imaging procedures were statistically significant indicators of acute SAH ($p < 0.05$). In the detection of subacute-to-chronic SAH (> 5 days post-ictus), GE T2*-weighted images had significant advantages over other MRI pulse sequences and CT ($p = 0.001$). The reason for this superiority is that GE T2*-weighted images are very sensitive to the paramagnetic by-products of hemoglobin.

When massive bleeding occurs in acute SAH, a stronger than previously described T2-shortening effect is observed;[5,6,16] the area of marked T2 shortening is due to heavily packed RBCs, which may be shielded from CSF and result in high hematocrit and increased deoxyhemoglobin formation. These aspects of SAH are demonstrated as areas of decreased signal intensity and are not easily detected on FLAIR images.

The hyperintense CSF depicted on FLAIR images may be seen in conditions other than SAH.[13] For example, severe purulent meningitis, granulomatous meningitis, arachnoiditis, meningeal metastasis or CSF dissemination of primary brain tumors, such as germinoma, ependymoma, medulloblastoma, or glioblastoma, may result in increased CSF signal intensity on FLAIR images. A ruptured dermoid is also a potential simulator of SAH on FLAIR images because of the short T1 of its fat component. These conditions should be distinguishable from SAH based on clinical information and/or using fat-saturation contrast material-enhanced MRI.

As stated above, GE T2*-weighted images are very sensitive to the paramagnetic by-products of hemoglobin, such as ferrous (Fe^{2+}) and ferric (Fe^{3+}) ions. Iron in the form of Fe^{2+} or Fe^{3+} ions is paramagnetic,[1] and the presence of paramagnetic species in the CSF leads to localized perturbations in the magnetic field. This leads to an increased precession rate in the immediate vicinity of ferrous or ferric ions on the atomic scale and, hence, a faster dephasing and loss of T2* signal as dark areas on T2*-weighted images. GE sequences with significant T2*-weighting are particularly sensitive to such localized changes and are, thus, well suited to the detection of SAH (Figure 3). The pitfall of GE T2*-weighted images is the marked difference in magnetic susceptibility between the skull and brain. SAH that occurs mostly on the brain surface and skull base might be hidden by the "blooming" artifacts produced at the interface of bone and brain tissues with different magnetic susceptibilities.[17]

An obvious limitation of this study is the small number of patients, especially those with acute-stage illness within 3 days of SAH. Various distinguishing times between "acute" and "subacute-chronic" SAH have been documented in the literature: for example, 3 days;[3] 4 days;[1] and 6 days.[18] Ogawa et al[3] reported the following detection rates for subacute-to-chronic SAH (4–75 days post-ictus): 63% and 25% for T1- and T2-weighted images, respectively, using a superconductive 0.5-T MRI unit; and 46% for CT. Mitchell et al[1] reported detection rates for acute SAH (≤ 4 days post-ictus) of 50% for T1-weighted images, 56% for T2-weighted images, 81% for FLAIR, and 94% for GE T2*-weighted images, using a 1.5-T MRI unit, and a detection rate of 95% for CT; corresponding detection rates for subacute SAH were 33%, 47%, 87%, 100%, and 75%. For patients with acute SAH defined as being within 6 days of ictus, Chrysikopoulos et al[18] reported MRI detection rates using a 0.5-T unit of 29% (T1-weighted images), 14% (T2-weighted images), and 71% (FLAIR); and a CT detection rate of 71%.

Different rates of positive SAH detection in the literature would be expected between CT and the various MRI pulse sequences studied because of the different parameters used and the different distinguishing times used to define acute and subacute-to-chronic SAH. Our distinguishing time was the fifth day because only 7 patients were in the acute-stage category of ≤ 3 days post-ictus. One false-negative CT case in our study was documented on the fifth day after ictus, which possibly explains why the rate of detection of

acute SAH (≤ 5 days post-ictus) was lower for CT than FLAIR (91% vs 100%). However, if a distinguishing time of ≤ 3 days post-ictus had been used to define acute SAH, the detection rate with CT would have been similar to that with FLAIR imaging.

In conclusion, CT is a sensitive and specific method for detecting acute SAH, but is insensitive for detecting subacute-to-chronic SAH. MRI methods, particularly FLAIR and GE T2*-weighted images, can perhaps support CT in the latter situation. The detection rate of SAH varied between the 4 MRI pulse sequences studied and CT. FLAIR and GE T2*-weighted MRI pulse sequences and CT were statistically significant indicators of acute SAH. GE T2*-weighted images were statistically significant indicators of subacute-to-chronic SAH, but other MRI pulse sequences and CT were not.

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