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Original Article

Diagnostic accuracy of flair in detection of acute subarachnoid hemorrhage in patients presenting with severe headache

Rabia Ashraf[d,*], Muhammad Akhtar[a], Sohail Akhtar[b], Iqra Manzoor[c]

[a] Department of Radiology, PNS Shifa, Karachi, Pakistan
[b] Department of Radiology, CMH, Nowshera, Pakistan
[c] University Institute of Radiological Sciences and MIT, The University of Lahore, Lahore, Pakistan
[d] Department of Radiology, 49, F1 Wapda Town, 54000 Lahore, Pakistan

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ABSTRACT

Background. – Fluid attenuation inversion recovery (FLAIR) magnetic resonance imaging (MRI) sequences are previously described for the evaluation of acute subarachnoid hemorrhage (SAH) and demonstrated good sensitivity. This study was designed to find the diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache considering the fact that controversy has been observed in previous studies.
Objective. – To determine diagnostic accuracy of FLAIR in detection of acute subarachnoid hemorrhage in patients presenting with severe headache using lumber puncture as gold standard.
Methodology. – A total of 245 patients fulfilling selection criteria were enrolled in the study through the emergency department of Combined Military Hospital, Lahore. MRI was performed by Philips Intera Achieva 1.5 T super conducting MR unit (Philips Medical Systems, the Netherlands), with the use of a head coil. FLAIR examination was performed at 6700/150 (TR/TE) with an inversion time (TI) of 2200 ms, a field of view 230 mm, matrix 189 × 256, scan time of 3 min 50s and section thickness 5 mm in axial plane. Following MRI, patients underwent lumbar puncture for cerebrospinal fluid (CSF) examination after 8–12 h from the onset of event. MRI and CSF analysis results were then compared.
Results. – Out of 245 cases, 49.39% ($n = 121$) were between 20–55 years of age while 50.61% ($n = 124$) were between 56–70 years of age, mean ± sd was calculated as 52.13 ± 10.45 years, 53.88% ($n = 132$) were male while 46.12% ($n = 113$) were females, frequency of acute subarachnoid hemorrhage in patients presenting with severe headache was recorded as 5.71%($n = 14$), diagnostic accuracy of FLAIR in detection of acute subarachnoid hemorrhage in patients presenting with severe headache taking lumbar puncture as gold standard as 78.57% sensitivity, 96.53% specificity, 57.89% positive predictive value, 98.67% negative predictive value and accuracy rate was calculated as 95.29%.
Conclusion. – Diagnostic accuracy of FLAIR in detection of acute subarachnoid hemorrhage in patients presenting with severe headache taking lumbar puncture as gold standard is higher and reliable.

Introduction

Headache is a common presenting complaint in the emergency department (ED), responsible for approximately 2% of all visits. Of these patients, about 1% will have subarachnoid hemorrhage (SAH) [1]. In the subset of patients who present with a severe, sudden onset, or "thunderclap," headache and a normal neurological examination, 10% to 16% will have SAH [2]. Overall, SAH mortality is approximately 40% at 1 week, with 10% to 15% of deaths occurring pre-hospital and 25% occurring within 24 hours of initial bleeding [3]. SAH is the extravasation of blood into the cerebrospinal fluid (CSF) and results from rupture of corticomeningeal vessels and from hemorrhagic contusions of the brain. SAH occurs with an annual incidence of approximately eight people per 100,000 population per year [4]. Other important causes include vascular malformations, vasculitis, cavernous angiomas, neoplasms, mycotic aneurysms, blood dyscrasias, intraparenchymal hematomas, trauma, and peri mesencephalic hemorrhage. Timely diagnosis of SAH in the ED is paramount because failure to reach the diagnosis in a prompt manner can lead to many

* Corresponding author.
E-mail addresses: drrabiaashraf39@gmail.com (R. Ashraf), drawanma@gmail.com (M. Akhtar), sohail.gc@hotmail.com (S. Akhtar), iqramanzoor36@gmail.com (I. Manzoor).

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complications [5]. Computed tomography (CT) followed by lumbar puncture (LP) is a time-honored practice. CT is the preferred method for routine imaging of patients with suspected SAH due to its high sensitivity and wide availability because CT is automated high-speed system for production process control and optimization [6]. Until recently, traditional T1- and T2-weighted MRI was thought to be less sensitive for detection of SAH. However, recent studies have demonstrated that fluid attenuation inversion recovery (FLAIR) MRI is equal to or even more sensitive than CT for detection of acute or subacute SAH [7]. CT also has key limitations, including lower sensitivity in the posterior fossa due to beam-hardening artifacts. Other limitations to CT include its use in patients with normal neurological examinations and smaller volumes of hemorrhage who are less likely to have CT abnormalities [8]. Lumbar puncture (LP) remains the standard of care for ruling out SAH when non-contrast head CT is negative [9]. In a study including 50 patients considering LP as gold standard, the sensitivity for the diagnosis of acute SAH by FLAIR MRI was 97.6%, however specificity was lower (66.7%) [10]. However, a similar study ($n = 25$) showed that sensitivity and specificity of SAH detection by FLAIR were 58.3% and 89.4%, respectively [11]. Headaches attributed to disorders of homeostasis were referred to as "headaches associated with metabolic or systemic diseases" in the first edition of the International Headache Society International Classification of Headache Disorders (ICHD)-1.12 The recent third edition the ICHD-3 (beta version), states that if a headache occurs for the first time in close temporal relation to a disorder of homeostasis, it is coded as a secondary headache attributed to that disorder. ICHD-3 beta includes headaches attributed to [1] hypoxia and/or hypercapnia (high altitude, diving, and sleep apnea), [2] dialysis, [3] arterial hypertension (pheochromocytoma, hypertensive crisis without hypertensive encephalopathy, hypertensive encephalopathy, preeclampsia or eclampsia, and autonomic dysreflexia), [4] hypothyroidism, [5] fasting, [6] cardiac cephalalgia, and [7] other disorder of homeostasis [12]. Non-emergent headaches are of following types including: hypoxia/hypercapnia, migraine headache, tension headache, trigeminal neuralgia. While emergent headaches are: subdural hematoma, vasculitis, cerebrovascular accident, encephalitis, meningitis, and SAH. The frequency of ruptured and unruptured aneurysms has been estimated at 1–9% in different autopsy series, with a prevalence of unruptured aneurysms of 0.3–5%. Retrospective arteriographic studies show a prevalence of less than 1% with the limitation that some cases did not receive adequate evaluation and thus some aneurysms may have been missed. Annual incidence increases with age and probably is underestimated because death is attributed to other reasons that are not confirmed by autopsies [13]. The annual incidence of aneurysmal SAH in the United States is 6–16 cases per 100,000 population, with approximately 30,000 episodes occurring each year. Unlike other subcategories of stroke, the incidence of SAH has not decreased over time. However, population-based survival rates have improved [14]. The reported incidence of SAH is high in the United States, Finland, and Japan, while it is low in New Zealand and the Middle East. In Finland, the estimated incidence based on different studies is 14.4–19.6 cases per 100,000 population, although numbers as high as 29.7 have been reported [15]. In Japan, the reported rates vary between 11 and 18.3 cases per 100,000 population, with one study showing an incidence of 96.1 cases per 100,000 population (this study included only patients aged 40 and older in the data collection, and results were not adjusted for sex and age to the same reference population) [16]. In New Zealand, age-adjusted incidence was reported as 14.3 cases per 100,000 inhabitants. An Australian study reported an incidence of 26.4 cases per 100,000 population but only for patients older than 35 years, as age was not adjusted in the reference population [17]. Iceland reported 8 cases per 100,000 population, but a significant portion of the affected rural population was believed to be missed [18]. Greenland Eskimos had 9.3 cases per 100,000 population; ethnic Danes there had an incidence of 3.1 cases per 100,000 population. This latter figure is consistent with the figures in Denmark—marked differences are postulated to be related to genetic factors. On the Faeroe Islands (part of Denmark with an isolated population of the same genetic ancestry), the reported incidence is 7.4 cases per 100,000 population [19]. In China, the reported incidence is low, but no good studies have been published to support this statement [20]. The incidence among Indians is significantly lower than in those from European nations; this can be explained partly by the low incidence of atherosclerosis in these populations [21]. The risk is higher in blacks than in whites; however, people of all ethnic groups develop intracranial aneurysms. The disparity in frequency of rupture has been attributed to population variance with respect to prevalence of risk factors and age distribution [14]. The incidence of SAH in women is higher than in men (ratio of 3 to 2). The risk of SAH is significantly higher in the third trimester of pregnancy, and SAH from aneurysmal rupture is a leading cause of maternal mortality, accounting for 6–25% of maternal deaths during pregnancy. A higher incidence of AVM rupture also has been reported during pregnancy [13]. Incidence increases with age and peaks at age 50 years. Approximately 80% of cases of SAH occur in people aged 40–65 years, with 15% occurring in people aged 20–40 years. Only 5% of cases of SAH occur in people younger than 20 years. SAH is rare in children younger than 10 years, accounting for only 0.5% of all cases [22]. The rationale of this study is to find the diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache. Controversy has been observed in previous studies as mentioned above. But this ambiguity may be due to small sample size. Larger studies and clinical trials are needed in order to include FLAIR MRI as an integral part examination of the patient during an acute event of any suspected acute SAH because in addition to pick even smaller SAH, it's the valuable modality to comment on the cause of SAH. So, we conducted this study on large sample size to get more reliable results. Furthermore, we implemented the use of FAIR and can replace CT and its harmful radiations. The results of this study can help in improving our practice and guidelines for detection of SAH in headache patients through FLAIR instead of other modalities, which may also prevent loss of time in such delicate case.

Material and methods

It was a cross-sectional study on diagnostic accuracy of flair in detection of acute SAH in patients presenting with severe headache. Two hundred and forty five patients were enrolled in this study with non-probability, consecutive sampling technique. The study was carried out in Radiology department of Combined Military Hospital (CMH), Lahore, Pakistan. The duration of the study was from 5th October 2015 to 5th April 2016. Patients of age 20–70 years, of either gender presenting in ED with acute severe headache (pain on VAS > 6) with nausea, vomiting, neck pain, photophobia, loss of consciousness or Glasgow coma scale < 13 were included in the study. Patient with history of trauma and intracranial tumors (on medical record and clinical examination), patients who had previous history of intracranial hemorrhage (medical record), uncooperative and non-willing patients were excluded from the study. After taking permission from hospital ethical committee, 245 patients fulfilling selection criteria were enrolled in the study through ED of CMH Hospital, Lahore. Written informed consent was taken. Demographic detail (name, age, sex, duration of headache) was also noted. Then MRI imaging was performed by Philips Intera Achieva 1.5 T super conducting MR unit (Philips Medical Systems, the Netherlands), with the use of head coil. FLAIR examination

Table 1
Age distribution.

Age (in years)	No. of patients ($n = 245$)	%
20–55	121	49.39
56–70	124	50.61
Total	245	100
Mean ± SD	52.13 ± 10.45	

Table 2
Gender distribution.

Gender	No. of patients ($n = 245$)	%
Male	132	53.88
Female	113	46.12
Total	245	100

Table 3
Frequency of acute subarachnoid hemorrhage in patients presenting with severe headache.

SAH	No. of patients ($n = 245$)	%
Yes	14	5.71
No	231	94.29
Total	245	100

was performed at 6700/150 (TR/TE) with an inversion time (TI) of 2200 ms, a field of view 230 mm, matrix 189 × 256, scan time of 3 min 50s and section thickness 5 mm in axial plane. Patients had as positive or negative. Then these patients were submitted finally to LP for CSF examination after 8–12 h from the onset of event. Reports of both procedures were compared for final decision. All this information was recorded in proforma. All the collected data was entered and analyzed through SPSS version 20. Quantitative data like age and duration of headache was presented as mean and standard deviation. Qualitative data like gender and SAH (present or absent) on FLAIR and LP was presented as frequency and percentage. A 2 × 2 table was generated to calculate sensitivity, specificity, PPV, NPV and diagnostic accuracy of FLAIR taking LP evaluation as gold standard. The data was stratified for age, gender and duration of headache to address the effect modified. Past-stratification Chi^2 test was applied with P-value < 0.05 as significant.

Results

A total of 245 cases fulfilling the inclusion/exclusion criteria were enrolled to find the diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache taking LP as gold standard. Age distribution of the patients was done showing that 49.39% ($n = 121$) were between 20–55 years of age while 50.61% ($n = 124$) were between 56–70 years of age, mean ± sd was calculated as 52.13 ± 10.45 years (Table 1). Patients were distributed according to gender showing that 53.88% ($n = 132$) were male while 46.12%($n = 113$) were females (Table 2). Frequency of acute SAH in patients presenting with severe headache was recorded as 5.71% ($n = 14$) while 94.29% ($n = 231$) had no findings of the morbidity (Table 3). Diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache taking LP as gold standard as 78.57% sensitivity, 96.53% specificity, 57.89% positive predictive value, 98.67% negative predictive value and accuracy rate was calculated as 95.29% (Table 4). Stratification for age and gender was done and presented in Table 5a, Table 5b, Table 6a and Table 6b respectively.

Table 4
Diagnostic accuracy of flair in detection of acute subarachnoid hemorrhage in patients presenting with severe headache taking LP as gold standard ($n = 245$).

FLAIR	Lumbar Puncture		Total
	SAH (Positive)	SAH (Negative)	
Positive	True positive (a) 11 (4.49%)	False positive (b) 8 (11.84%)	a + b 19(7.75%)
Negative	False negative (c) 3 (1.22%)	True negative (d) 223 (82.45%)	c + d 226 (%)
Total	a + c 14 (5.71%)	b + d 231 (94.29%)	245 (100%)

Table 5a
Stratification for age (Age: 20–55 years).

FLAIR	Lumbar Puncture ($n = 121$)		P-value
	SAH (Positive)	SAH (Negative)	
Positive	True positive (a) 5	False positive (b) 3	0.000
Negative	False negative (c) 2	True negative (d) 111	
Total	a + c 7	b + d 114	

Table 5b
Stratification for age (Age: 56–70 years).

FLAIR	Lumbar Puncture ($n = 124$)		P-value
	SAH (Positive)	SAH (Negative)	
Positive	True positive (a) 6	False positive (b) 5	6.97
Negative	False negative (c) 1	True negative (d) 112	
Total	a + c 7	b + d 117	

Table 6a
Stratification for gender (Male).

FLAIR	Lumbar Puncture ($n = 132$)		P-value
	SAH (Positive)	SAH (Negative)	
Positive	True positive (a) 4	False positive (b) 6	0.000
Negative	False negative (c) 1	True negative (d) 121	
Total	a + c 5	b + d 127	

Table 6b
Stratification for gender (Female).

FLAIR	Lumbar Puncture ($n = 113$)		P-value
	SAH (Positive)	SAH (Negative)	
Positive	True positive (a) 7	False positive (b) 2	6.97
Negative	False negative (c) 2	True negative (d) 102	
Total	a + c 9	b + d 104	

Discussion

Fluid attenuation inversion recovery (FLAIR) MR imaging sequences are previously described for the evaluation of acute SAH and demonstrated good sensitivity. This study was designed to find the diagnostic accuracy of FLAIR in detection of acute SAH

in patients presenting with severe headache considering the fact that controversy has been observed in previous studies. In our study, out of 245 cases, 49.39% ($n = 121$) were between 20–55 years of age while 50.61% ($n = 124$) were between 56–70 years of age, mean ± sd was calculated as 52.13 ± 10.45 years, 53.88% ($n = 132$) were male while 46.12% ($n = 113$) were females, frequency of acute SAH in patients presenting with severe headache was recorded as 5.71% ($n = 14$), diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache taking LP as gold standard as 78.57% sensitivity, 96.53% specificity, 57.89% positive predictive value, 98.67% negative predictive value and accuracy rate was calculated as 95.29%. We compared our study with a previous study including 50 patients considering LP as gold standard; the sensitivity for the diagnosis of acute SAH by FLAIR MRI was 97.6% however lower specificity (66.7%) [10]. Our findings are not in agreement with the above study, as we recorded more accuracy in specificity and comparatively lower sensitivity. Another study ($n = 25$) showed that sensitivity and specificity of SAH detection by FLAIR were 58.3% and 89.4%, respectively [11]. Our findings are in agreement with this study regarding specificity while higher sensitivity as reported in the above study. On the other hand, another study by Richard, J and co-workers recorded the sensitivity of FLAIR was 89%, which is in agreement with our study. They concluded that FLAIR was more sensitive than CT in the evaluation of acute SAH in this model, especially when a high volume of SAH was present [23]. Verma RK and others 84 compared the utility of susceptibility weighted imaging (SWI) with the established diagnostic techniques CT and fluid attenuation inversion recovery (FLAIR) in their detecting capacity of SAH, and further to compare the combined SWI/FLAIR MRI data with CT to evaluate whether MRI is more accurate than CT, they recorded that SAH was detected in a total of 146 subarachnoid regions. CT identified 110 (75.3%), FLAIR 127 (87%), and SWI 129 (88.4%) involved regions. Combined FLAIR and SWI identified all 146 detectable regions (100%). FLAIR was sensitive for frontal-parietal, temporal-occipital and Sylvian cistern SAH, while SWI was particularly sensitive for interhemispheric and intraventricular hemorrhage. They concluded that by combining SWI and FLAIR, MRI yields a distinctly higher detection rate for SAH than CT alone, particularly due to their complementary detection characteristics in different anatomical regions. Detection strength of SWI is high in central areas, whereas FLAIR shows a better detection rate in peripheral areas. Though the combined FLAIR/SWI was showing good results but alone FLAIR also detected 87% of the cases, which shows higher sensitivity. However, in this study on large sample size we got more reliable results. Furthermore, these results enabled us to implement the use of FAIR and it can replace CT and its harmful radiations. The results of this study are helpful for us in improving our practice and guidelines for detection of SAH in headache patients through FLAIR instead of other modalities, which may also prevent loss of time in such delicate case.

Conclusion

We concluded that the diagnostic accuracy of FLAIR in detection of acute SAH in patients presenting with severe headache taking LP as gold standard is higher and reliable but some-other local trials are also required to validate our findings.

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Disclosure of interest

The authors declare that they have no competing interest.

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