

Role of Diffusion-weighted Imaging in Detecting Early Ischemic Brain Injury Following Aneurysmal Subarachnoid Hemorrhage

Abstract

Background: Aneurysmal SAH is the significant cause of morbidity and mortality in stroke patients. Early brain injury and delayed cerebral ischemia are the two main responsible pathophysiologic processes. Cerebral ischemia needs to be detected early so that early aggressive therapy could be started. Although Diffusion weighted imaging (DWI) has often been utilized for the measurement of acute ischemic strokes, its role in the detection of early cerebral ischemia due to aneurysmal subarachnoid hemorrhage has not been extensively investigated. This study is being carried out to describe the role of DWI in detecting early ischemic brain injury and outcome after aneurysmal SAH. **Aim:** Efficacy of DWI in detecting ischemic injury and predicting outcome after aneurysmal SAH. **Material and Methods:** In this prospective study 44 consecutive patients who had aneurysmal SAH; admitted within 7 days of their ictus were included. Hunt and Hess grade on admission and modified Fisher grade of SAH were noted. Plain CT brain and MR DWI was done on day before surgery. Diffusion restriction on DWI was correlated with postoperative neurological deficit, postoperative CT finding and outcome of the patient at 1 month follow-up. **Results:** DWI revealed restricted diffusion in 12 patients, out of which 1 patient was having infarction in preoperative CT scan, 6 patients were having postoperative deficit in the form of disorientation, hemiparesis and aphasia, and all patients were having infarction in postoperative CT scan. When DWI findings were compared on the basis of postoperative neurological deficit, postoperative CT finding and modified Rankin outcome score at 1 month follow-up, results were statistically significant. **Conclusion:** DWI shows cerebral ischemia much earlier than CT scan in cases of aneurysmal SAH. It has significant correlation with postoperative neurological status and outcome of the patient.

Keywords: Diffusion-weighted imaging, hemorrhage subarachnoid, Hunt and Hess grade

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is the significant cause of morbidity and mortality in stroke patients.^[1] Early brain injury and delayed cerebral ischemia are the two main responsible pathophysiologic processes. Vasospasm, initial transient global ischemia, intracerebral hematoma, meningitis, increasing age, premorbid disease, and electrolyte imbalance are the important causes of cerebral ischemia. Although angiographic vasospasm is seen in 60%–70% patients, clinical vasospasm is seen in only one-third of them.^[2] Silent ischemic events are well known during diagnostic and therapeutic endovascular procedures, but in cases of microsurgical clipping, it needs to be evaluated. Although the patient's neurological examination may be normal, a number of radiologic tools are under trial to detect these silent ischemic events as soon as possible. A number of

studies have shown the effectiveness of diffusion-weighted MRI (DWI) in the early detection of ischemic brain injury wherein diffusion of water protons is decreased because of cytotoxic edema in the acute ischemia (thus appearing bright on DWI).^[3,4] Although DWI has often been utilized for the measurement of acute ischemic strokes, its role in the detection of early ischemic events due to aneurysmal SAH has not been extensively investigated in the study. This study is being carried out to describe the role of DWI in detecting early ischemic brain injury after aneurysmal SAH so that early intervention could be done to restrict further damage.

Materials and Methods

This prospective study was conducted between December 2015 and 2016 in 44 consecutive patients (male: female ratio 1:1.2; mean age 48.48 ± 12.6 years) who had aneurysmal SAH; admitted within

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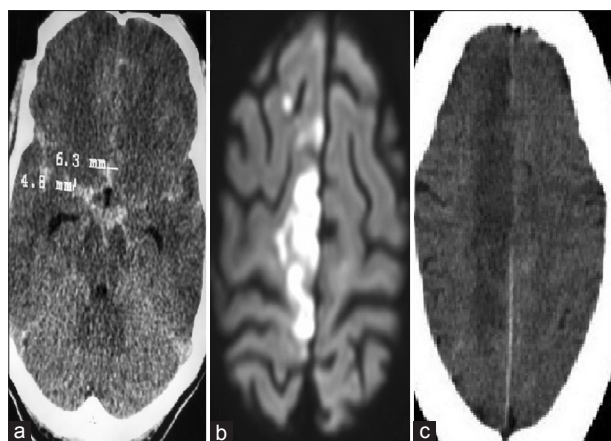


Figure 1: (a) Preoperative computed tomography scan of a patient showing subarachnoid hemorrhage with ruptured anterior communicating artery aneurysm. (b) Diffusion-weighted imaging showing diffusion restriction. (c) Postoperative computed tomography scan showing the right anterior cerebral artery infarct

7 days of their ictus. The patients having intracerebral hematoma, those in Hunt and Hess (H and H) Grade V, those having metallic implants in body, and those having digital subtraction angiography after preoperative MRI study were excluded from the study. On the basis of clinical condition of the patient on admission, H and H grade and World Federation of Neurosurgeons grade were noted. SAH was determined on the basis of computed tomography (CT) scan and graded according to modified Fisher scale. CT angiogram was done on Philips 128 slice multi-detector CT scanner to know the size, number, location, direction, and morphology of aneurysm. Using 3 Tesla Philips superconducting Signa MRI units, axial T1-weighted (T1W), T2-weighted (T2W), and diffusion weighted images were obtained and areas of hyperintense signal on DWI were noted. All MRI studies were evaluated by radiologist for detection of signs of ischemia. The treating surgeon was not aware of DWI findings and radiologist who reported the imaging was not aware of clinical status of the patient.

All the patients received in the early stage of SAH were given triple H therapy and oral nimodipine to prevent vasospasm. Plain CT brain and MRI brain with diffusion-weighted imaging were performed on the day before surgery, and the areas of ischemia represented by hyperintense signal were noted. There were 7 patients of internal carotid artery aneurysm, ten middle cerebral artery aneurysm, twenty anterior communicating artery (A.COM) aneurysm, 6 distal cerebral artery aneurysm, 3 posterior communicating artery aneurysm, 2 basilar top aneurysm, and 3 patients of multiple aneurysm. The patients were treated with microsurgical clipping ($n = 31$) or endovascular coiling ($n = 13$). A postoperative CT scan was done within 5 days of surgery and areas of infarction were noted. Regular hemodynamic and neurological monitoring was done during the hospital stay. Modified Rankin score was

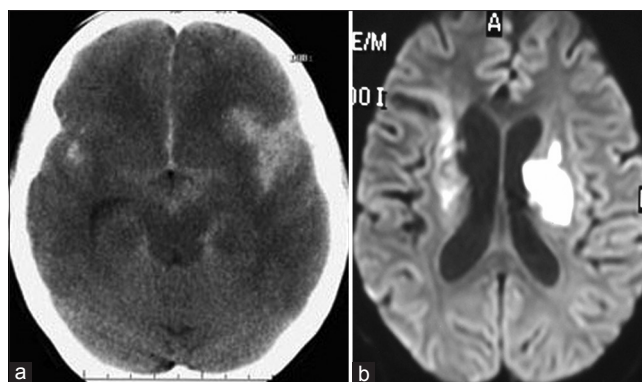


Figure 2: (a) Preoperative computed tomography scan showing the left middle cerebral artery aneurysmal bleed. (b) Diffusion-weighted imaging showing diffusion restriction

determined at 1-month follow-up and graded as good when the patient was independent for daily activities and poor when patient was dependent on others for daily needs.

The areas of ischemia seen on MR images were correlated with the clinical condition, both pre- and post-operative CT scan and clinical outcome of the patient. The efficacy of DWI in predicting outcome at a mean follow-up of 1 month was determined. The statistical analysis of findings on MR DWI, CT scan, and clinical findings was done.

The Ethical Committee clearance was taken from the Institute Ethics Committee, and written informed consent was taken from all the patients included in the study.

Statistical analysis

Statistical analysis was performed with the SPSS, Trial Version 23 for Windows statistical software package (SPSS inc., Chicago, USA) and Primer. The categorical data were presented as numbers (percentage) and were compared among groups using Chi-square test. The quantitative data were presented as mean and standard deviation and were compared using Student's *t*-test, and correlation analysis was performed using Pearson correlation coefficient ($r =$ at least 0.8 very strong, 0.6 up to 0.8 moderately strong, 0.3–0.5 good and <0.3 is poor). $P < 0.05$ was considered statistically significant.

Results

DWI revealed restricted diffusion in 12 patients, out of which 1 patient was having infarction in preoperative CT scan, 7 patients were having postoperative deficit in the form of disorientation, hemiparesis and aphasia, and all patients were having infarction in postoperative CT scan [Tables 1 and 2]. Out of 5 patients who got expired 4 were having diffusion restriction on DWI. The distribution of the ischemic lesions was confined to the vascular territory of perforating arteries in most of the cases [Figures 1 and 2].

H and H grade on admission and modified Fisher grade were having significant correlation with modified Rankin outcome

score of the patient. When DWI findings were compared on the basis of postoperative neurological deficit, postoperative CT finding and modified Rankin outcome score at 1-month follow-up, results were statistically significant [Table 3].

Discussion

Aneurysmal SAH accounts for 85% cases of spontaneous SAH and rest are due to nonaneurysmal perimesencephalic SAH, postinfectious, tumoral bleed, and hematologic disorders.^[1] The incidence increases with age and peak incidence age is 50–60 years. Aneurysmal SAH is 1.6 times more common in women; this preponderance increases after the fifth decade.^[5] The pathophysiologic consequences of aneurysmal SAH depend on the volume and location of the bleeding, patient’s age, clinical condition on admission and premorbid disease. Early brain injury and delayed cerebral ischemia are the two pathophysiologic processes that determine the outcome of aneurysmal SAH. Early brain injury results from raised intracranial pressure (ICP) and transient global ischemia

which triggers a cascade of pathophysiologic processes including inflammation, cortical spreading depression, capillary thrombosis, blood–brain barrier dysfunction, cerebral edema, and neuronal apoptosis.^[6] Delayed cerebral ischemia has a number of causes, foremost important is vasospasm, then increased cerebral edema (surrounding intracerebral hematomas, contusions, or infarcts), rebleeding of the aneurysm, sepsis (including meningitis and ventriculitis), hypoxia and hypotension. Vasospasm is of two types: angiographic and symptomatic and peaks during 6–14 days of aneurysmal SAH. Vasospasm occurs in about one-third cases of aneurysmal SAH as a response of intracranial arteries to cisternal accumulation of blood. In approximately 10% of cases, the vasospasm becomes symptomatic with permanent neurological deficits related to cerebral infarct. Euvolemia, normotension, hemodilution, oral nimodipine, and electrolyte balance are the strategies to prevent vasospasm. The exact volume of infarct is dependent on many factors: duration and degree of ischemia, prior status of cerebral ischemia, completeness of circle of Willis, development of leptomeningeal collaterals, and hemodynamic status of the patient.^[7] CT perfusion scanning, MR perfusion imaging and MR DWI imaging are the investigations used to detect early cerebral ischemia.^[8,9]

MR DWI lesions are commonly seen in infarction, cerebral abscess, tumors, and some nonneoplastic lesions. But when routine T1W, T2W and contrast studies are added; these lesions are easily differentiated. There are only a few studies that have evaluated cerebral ischemia with DWI in aneurysmal SAH.^[10,11] Soeda *et al.* evaluated 66 consecutive cases of asymptomatic aneurysm coil embolization with MR DWI. DWI images were done in all 66 patients at 2–5 days after embolization. They concluded that significant percentage of complex aneurysm cases having hyperintense lesion on DWI image deteriorated due to cerebral ischemia.^[12] In another study by Sakai *et al.*, they evaluated 137 patients who received 154 neurointerventional procedures and studied the diffusion-weighted images before and within 5 days after treatment. Diffusion-weighted imaging detected procedure-related lesions in 83 of 154 procedures (53.9%). Only 36 demonstrated no new neurological symptoms during and/or after the procedure.^[13] Condetta *et al.* studied the role of DWI in vasospasm after aneurysmal SAH in 7 patients with conclusion that it picks up early cerebral ischemia, although larger studies still needed to prove it.^[14] In 2008 Wani *et al.* studied, the role

Table 1: Relation between Hunt and Hess grade, computed tomography scan, diffusion-weighted imaging findings and postoperative deficit

H and H	Number of patients (n)	CT1 (n)	DWI (n)	CT2 (n)	Postoperative deficit (n)
1	31	0	7	7	2
2	6	0	1	1	1
3	3	0	1	1	1
4	4	1	3	3	3

H and H – Hunt and Hess grade; CT1 – Preoperative CT having infarct; DWI – Restriction in diffusion-weighted image; CT2 – Postoperative CT having infarct; CT – Computed tomography

Table 2: Relation between Modified Fisher Scale, computed tomography scan, diffusion-weighted imaging findings and postoperative deficit

Fisher	Number of patients (n)	CT1 (n)	DWI (n)	CT2 (n)	Postoperative deficit (n)
1	34	0	5	5	2
2	5	0	2	2	1
3	4	0	4	4	3
4	1	1	1	1	1

Fisher – Modified Fisher Scale; DWI – Restriction in diffusion-weighted image; CT1 – Preoperative CT having infarct; CT2 – Postoperative CT having infarct; CT – Computed tomography

Table 3: Correlation between diffusion-weighted imaging findings, mean hospital stay, postoperative deficit and Rankin outcome

DWI	Mean hospital stay	Postoperative deficit		Rankin outcome		
		Yes	No	Good	Poor	Dead
No restriction (n=32)	14.58±3.89	0	32	31	0	1
Restriction (n=12)	12.56±3.53	7	5	1	7	4
P	0.12 (NS)	<0.001 (S)		<0.001 (S)		

Rankin – Modified Rankin Scale; 0–2 – Good; 3–5 – Poor; NS – Not significant; S – Significant; DWI – Restriction in diffusion-weighted image

of DWI in predicting outcome in aneurysmal SAH due to A.COM artery aneurysm rupture. They studied 16 patients and found a positive correlation between DWI lesions and both radiological and clinical outcome of patients.^[15] DWI lesion strongly correlates with irreversible infarction, but there are few studies in animals showing reversibility of these ischemic lesions.

In our study, most of the patients were in good clinical grade (H and H 1 and 2) because poor grade patients were critically ill to be shifted for DWI study. Most of the patients who were in poor clinical grade (H and H 3 and 4) were having diffusion restriction on DWI, postoperative neurological deficit, and poor outcome. It may be due to large volume of SAH causing early brain injury, vasospasm and raised ICP, responsible for delayed cerebral ischemia. Out of 12 patients who were having diffusion restriction on DWI only one patient was having infarct on preoperative CT scan, and all 12 patients were having infarct on postoperative CT scan corresponding to DWI finding. There was no reversible lesion in our study although it was seen in few animal studies.^[15] Out of 12 patients having diffusion restriction, only seven patients were having postoperative deficit and five patients were having no deficit on routine neurological examination. Such silent ischemic events were reported in literature.^[15] Both number and size of DWI lesions were directly related to volume of SAH. Out of 5 patients who got expired 4 patients were having DWI lesions. Hence, DWI shows ischemia much earlier and we can start aggressive therapy much earlier to prevent further cerebral damage.

Conclusion

Diffusion restriction on DWI is more in poor clinical and poor SAH grade patients. DWI shows cerebral ischemia much earlier than CT scan in cases of aneurysmal SAH and has a significant correlation with postoperative neurological status and outcome of the patient. Hence, it is a valuable tool to reduce the morbidity and mortality of patients with aneurysmal SAH.

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Conflicts of interest

There are no conflicts of interest.

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