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Role of Diffusion-Weighted MRG in Predicting Outcome in Subarachnoid Hemorrhage Due to Anterior Communicating Artery Aneurysms

Anterior Komunikan Arter Anevrizmasına Bağlı Subaraknoid Kanamanın Prognozunun Belirlenmesinde Difüzyon MRG`nin Rolü

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ABSTRACT

AIM: Efficacy of DWI in detecting ischemic injury following anterior communicating artery aneurysmal SAH is studied

MATERIAL and METHODS: In this prospective study ,16 patients within 5 days of their ictus were included. Preoperative CT scan excluded an intracerebral infarct; an angiogram determined the extent of vasospasm; MR studies were done to detect cerebral ischemia and the diffusion coefficient (ADC) was calculated. Patients underwent surgery (n=12) or endovascular coiling (n=4). Postintervention CT scan within 24 hours and on day 5 determined radiological outcome as good or poor depending on the absence or presence of infarction. Clinical outcome at follow up (2-6 months) was regarded as good or poor when the patient was independent or dependent regarding daily activities, respectively,.

RESULTS: Restricted diffusion occurred in 8 (80%) of poor and in 1 (16.6%) of good grade patients ($p<0.05$). In patients with good radiological outcome (n=8), DWI restriction occurred in 2 (25%) patients. In patients with poor radiological outcome(n=8), DWI restriction occurred in 7 (87.5%) patients . At 2-6 month follow-up, 7 (77.8%) of 9 patients with restricted diffusion and 2 of 7 patients with no DWI abnormality showed a poor clinical outcome

CONCLUSION: Clinical and radiological outcome at follow-up is related to the preoperative DWI

KEY WORDS: Apparent diffusion, Radiological outcome, Subarachnoid hemorrhage

ÖZ

AMAÇ: Anterior komunikan arter anevrizmasına bağlı SAK sonrası gelişen iskemik hasarın belirlenmesinde DWI`in etkinliği çalışılmıştır.

YÖNTEM ve GEREÇLER: Bu prospektif calışmaya kanama sonrası ilk 5 gün içerisindeki 16 hasta dahil edilmiştir. Preoperatif BT intraserebral enfaktı ekarte etmek için; anjiyografi vazospazmın boyutunu belirlemek için; ve MR çalışması serebral iskemiyi belirlemek için yapılmıştır ve difüzyon katsayısı (ADC) hesaplanmıştır. Hastalar ameliyat edilmiştir (n=12) veya endovasküler koilleme yapılmıştır (n=4). Girişim sonrasi 24 saat içindeki ve 5. gündeki BT ile enfarkt varlığına veya yokluğuna göre radyolojik sonuç iyi veya kötü olarak belirlenmiştir. Takip esnasındaki (2-6 ay) klinik sonuç günlük aktivitelerindeki bağımlı veya bağımsız oluşuna göre iyi veya kötü olarak kabul edilmiştir.

Sonuçlar: Difüzyon kısıtlanması kötü gradeli hastaların 8`inde (80%) ve iyi gradeli hastaların 1`inde (16.6%) görülmüştür. Radyolojik sonucu iyi olan hastalarda (n=8) DWI kısıtlanması 2 hastada (25%) görülmüştür. . Radyolojik sonucu kötü olan hastalarda (n=8), DWI kısıtlanması 7 hastada (87.5%) görülmüştür. 2-6 aylık takipte difüzyon kısıtlamalı 9 hastanın 7`sinde (77.8%) ve DWI anormalliği olmayan 7 hastanın 2`sinde kötü klinik sonuç görülmüştür.

SONUÇ: Takiplerdeki klinik ve radyolojik sonuçlar preoperatif DWI ile ilişkilidir.

ANAHTAR SÖZCÜKLER: Diffüzyon MRG, Radyolojik sonuç, Subaraknoid kanama

INTRODUCTION

In aneurysmal subarachnoid hemorrhage, vasospasm causes significant morbidity. Although angiographic vasospasm is seen in 60 to 70% patients, clinical vasospasm (as evident by the emergence of focal neurological deficits or deterioration in the level of consciousness in the absence of intracerebral hematoma, infarction or biochemical alteration), is seen in only one third of them. [4] Diffusion weighted magnetic resonance imaging (DWI) is an important method of detecting early ischemic brain injury wherein diffusion of water protons is decreased because of cytotoxic edema in acute ischaemia (thus appearing bright on DWI). [13] As water protons diffuse and thus interact with the lattice and spin microenvironment, the proton displacement [expressed by an apparent diffusion coefficient (ADC)] is determined by their traveled path along any one direction per unit observation time. The decrease in the ADC of water after cerebral ischemia can be detected within minutes of the onset of ischemia. [18] When all other radiological investigations may be normal. Although DWI has often been utilized for the measurement of acute ischemic strokes, its role in the detection of early ischemia due to vasospasm following aneurysmal subarachnoid hemorrhage has not been extensively investigated .

In this study, we attempted to assess the efficacy of DWI in the preoperative detection of ischemia due to vasospasm following anterior communicating artery aneurysmal subarachnoid hemorrhage (SAH) and to compare its sensitivity to that of the conventional MR and CT scans.

MATERIAL & METHODS

This prospective study was carried out between February 2003 and July 2004, in 16 consecutive patients (male: female ratio 1:1.2; mean age 54.2 ± 3.1 years; age range 39-64 years) who had SAH due to rupture of anterior communicating artery aneurysm; and, who were admitted within 5 days of their ictus. Patients with intracerebral hematoma and those in Hunt & Hess grade V were excluded from the study. Six patients were in a good clinical grade (Hunt and Hess grade I and II) and 10 were in a poor clinical grade (Hunt and Hess III, IV). SAH was determined on the basis of a preoperative CT scan. On the same CT scans, it was also ascertained that none of the patients included in the study had an intracerebral infarct. A four-vessel cerebral angiogram was also performed and the extent of vasospasm noted. MRI studies were performed using 1.5 Tesla GE superconducting signa MRI unit (Signa GE Medical Systems). Axial T1 weighted images (imaging parameters TR= 600, TE=9.0, FOV=23.0?17.25, matrix=256?256/2) and axial T2 weighted images (imaging parameters FSE T2—TR=5500, TE= 82.0, FOV=23.0?17.25, matrix = 320?256/3) were obtained. A set of diffusion weighted images with B values 1000 & 0 were obtained in same image plan. On the preoperative DWI, the areas of ischemia represented by hyperintense signal and having an apparent diffusion coefficient (ADC) of less than 60% of normal values were noted. Areas in which ADC was more than 60% of normal values were disregarded as they may also represent other kinds of intra-voxel incoherent motions (IVIM) like capillary perfusion. [8, 9]

All patients underwent surgery (n=12) or endovascular coiling (n=4) using Gugleilmi detachable coils within 24 hours following the angiogram. A postoperative CT scan was done after 24 hours and on day 5 following the intervention. The presence of established infarction was noted in these scans. The radiological outcome was considered a good or a poor radiological outcome depending on absence or presence respectively, of infarction in the postoperative CT scan. The 3 mortalities in the series occurred in poor clinical grade patients due to extensive cerebral edema, pulmonary edema and acute respiratory distress syndrome respectively and occurred after more than 2 weeks following the surgical intervention.

The areas of ischemia seen on the preoperative MR images were correlated with the images seen on CT scan done on the postoperative day 1 and 5. The treating team was not aware of the MR findings. The radiologist who performed the MRI was not aware of the clinical status of the patients. The efficacy of DWI in predicting outcome at a mean follow up of 2-6 months was determined. The clinical outcome was taken as good when the patient was independent for daily activities, and poor when the patient was dependent on others for daily needs.

Statistical analysis:

The data was recorded on a spreadsheet in SPSS 10.0 software. Using Fischer exact test, the differences between good and poor radiological groups with relation to findings in DWI, T1W and

T2W MR scans, CT scan, and angiography were compared. A p value of <0.05 was taken as significant at 95% confidence interval.

RESULTS

DWI revealed the presence of restricted diffusion in 8 (80%) of the poor clinical grade patients and only in 1 (16.6%) of the good clinical grade patients (Table I). This difference was statistically significant ($p<0.05$).

In the patients with a good radiological outcome, (those who did not develop postoperative infarction; n=8), 5 (62.5 %) patients were in a good clinical grade (Hunt and Hess grade I and II) and 3 (37.5%) patients were in a poor clinical grade (Hunt and Hess grade III, IV). The angiogram revealed the presence of vasospasm in 2 (25%) patients. The preoperative DWI restriction was also noted in 2 (25%) patients. Their T1W and T2W images did not reveal any abnormality (Table II). These 2 patients with DWI restriction also had focal neurological deficits after the ictus and before the intervention, so triple –H therapy was started for them after surgery (Table I). None of them progressed to infarction in the postoperative period (Figure 4)

In the patients with a poor radiological outcome, (those who developed postoperative infarction n=8), only 1 (12.5%) patient was in a good clinical grade while 7 (87.5 %) patients were in a poor clinical grade. 4 (50%) patients had angiographic vasospasm and DWI restriction was noted in 7 (87.5%) patients

Table I: Table showing overview of patients included in the study.

n	DEFICIT (preop)	H & H	Fis	CT1	Avp	dw	T1W	T2W	triple-h	CT2	DEFICIT postop)
Good radiological outcome											
1	No	1	2	No	No	No	No	No	No	No	No
2	No	1	2	No	No	No	No	No	No	No	No
3	Rt.hemiparesis, aphasia	4	3	No	No	Lt.frontal pole, medial frontal	No	No	Yes	No	Decrease in weakness
4	No	1	2	No	BL.A1	No	No	No	No	No	No
5	No	1	1	No	No	No	No	No	No	No	No
6	No	2	3	No	No	No	No	No	No	No	No
7	Nil	4	4	No	Bl.a1	No	No	No	Yes	No	Died due to pulmonary edema
8	Rt.hemiparesis	4	4	No	No	Bl.medial frontal	No	No	Yes	No	No
Poor radiological outcome											
9	Lt.hemiparesis	4	2	No	Lt.a1,rt. m1	Bl.fronto-temporal Rt>lt	No	No	No	Small lt.frontal	No
10	Nil	3	4	No	No	No	No	No	Yes	Bl.aca,mca	Died due to extensive brain edema
11	Paraparesis	3	3	No	No	Bl.medial frontal	No	Yes	Yes	Bl.medial frontal	Subtle paraparesis
12	Rt.hemiparesis	4	3	Yes	Lt.a1	Bl.fronto-temporal	No	No	Yes	Lt mca,pca	No change in deficits
13	Lt.hemiparesis, aphasia	4	4	No	Bl.a1,2. lt.ica	Bl.frontal,lt.parietal	No	No	No	Lt.mca	No change in deficits
14	Rt.hemiplegia	4	4	No	Bl.a1,lt a2	Bl.posterior frontal lt>rt	No	Yes	Yes	Lt. aca, mca	Subtle weakness only
15	No	I	3	No	No	LT.posteriorfrontal	No	Yes	No	Lt. frontal	Rt. monoparesis
16	Aphasia,rt. hemiparesis	4	4	No	No	Lt.frontal	No	Yes	No	Lt.aca	Dead (ARDS)

CT1 = Infarct in preoperative ct scan, **DW**= Restriction in diffusion weighted images, **Avp**=Angiographic vasospasm **Fis**= Fischer grade, **CT2**=Infarct in postoperative ct scan, **BL**=Bilateral, **Rt**= Right, **Lt** = Left, **T I** =TI weighted MRI showing abnormality., **T2**= T2 weighted MRI showing abnormality.

Table II: Relation between radiological outcome and preoperative findings DWI,T1W,T2W and CT scan .

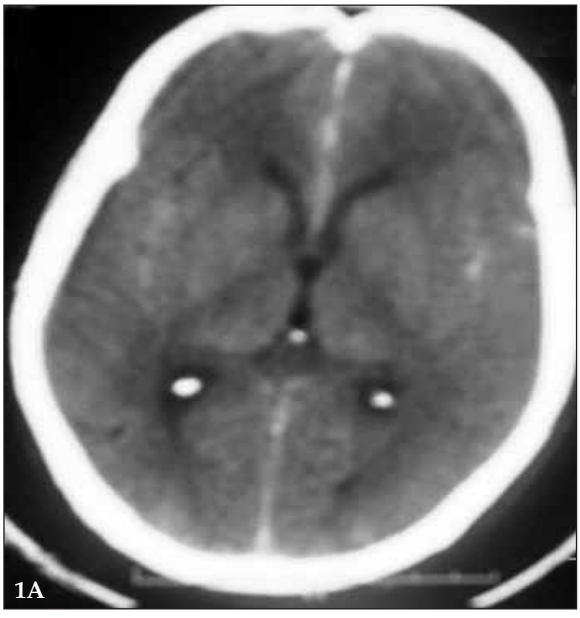
Radiologic al outcome (post op.)	DWI (restriction)		T1W abnormality		T2W abnormality		Vasospasm (Angiographic)	
	Yes	No	Yes	No	Yes	No	Yes	No
Good (no infarct) (N=8)	2	6	0	8	0	8	2	6
(%)	25.0	75.0	0	100.0	0	100.0	25.0	75.0
Poor (infarct) (N=8)	7	1	0	8	4	4	4	4
(%)	87.5	12.5	0	100.0	50.0	50.0	50.0	50.0
P value	**<0.05(S)**		>0.05(NS)		**<0.05(S)**		>0.05(NS)	

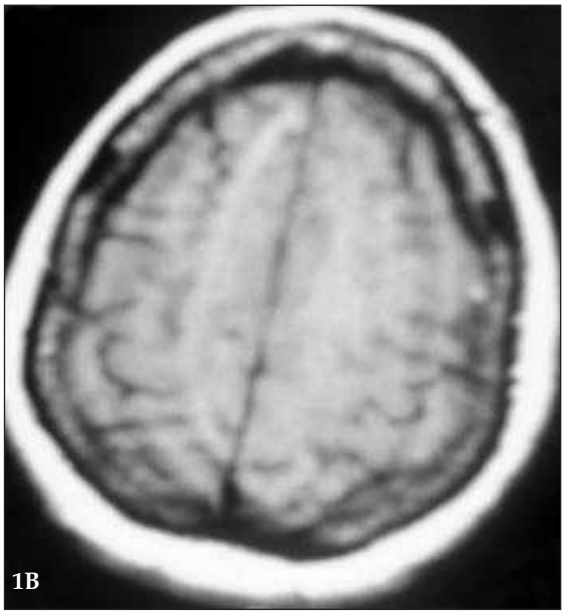
S-Statistically significant, NS-Statistically insignificant.

(Figure 1,2,3). T1W images did not reveal any abnormality. In T2W images, there was presence of hyperintensity in 4 (50%) patients. In this group triple–H therapy was instituted in 4 patients; however, all 8 of them progressed to infarction.

When the two groups (i.e., those with and without the presence of the infarct in the postoperative period) were compared, there was a statistically significant difference between them on basis of Hunt and Hess grade at admission ($p<0.05$), preoperative DWI restriction ($p<0.05$), and T2W abnormalities ($p<0.05$). There was no statistically significant difference in the two groups on the basis of angiogram findings (Table II).

Among the patients with DWI abnormalities (n= 9), preoperative focal neurological deficits were seen in 8 (88.9%) patients and no patient with normal DWI (n= 7) had focal neurological deficits and this





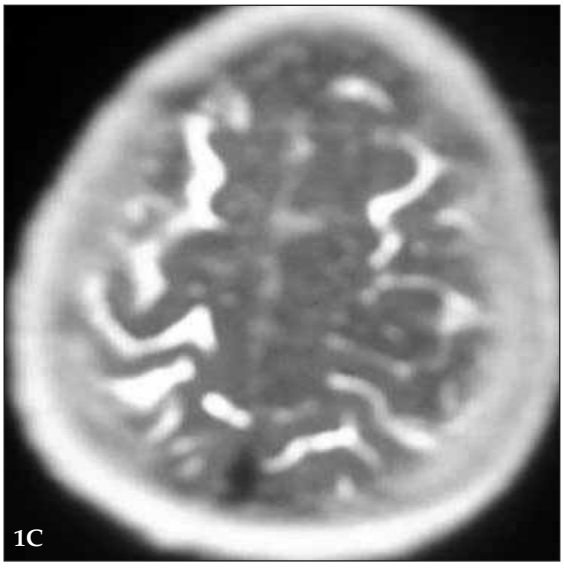


Figure 1: *Preoperative images of CT scan (**A**) T1W (**B**) and T2W (**C**) showing no infarct*

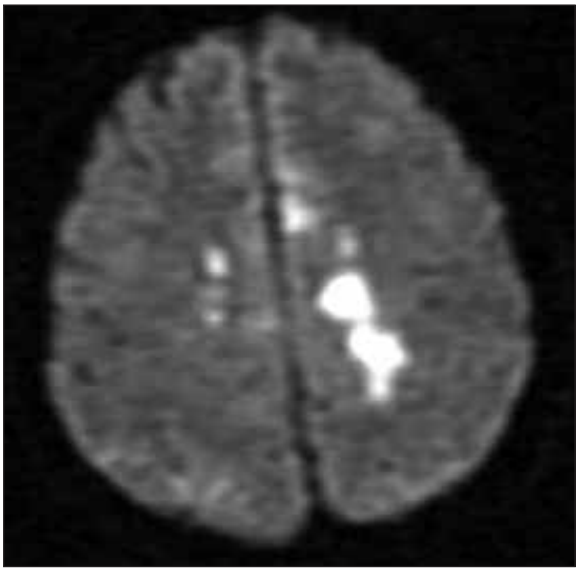


Figure 2: *Preoperative DWI showing restriction in posterior frontal region.*

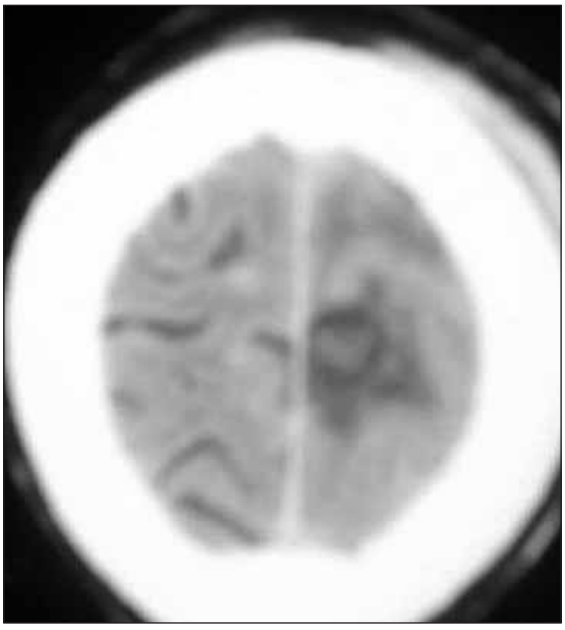
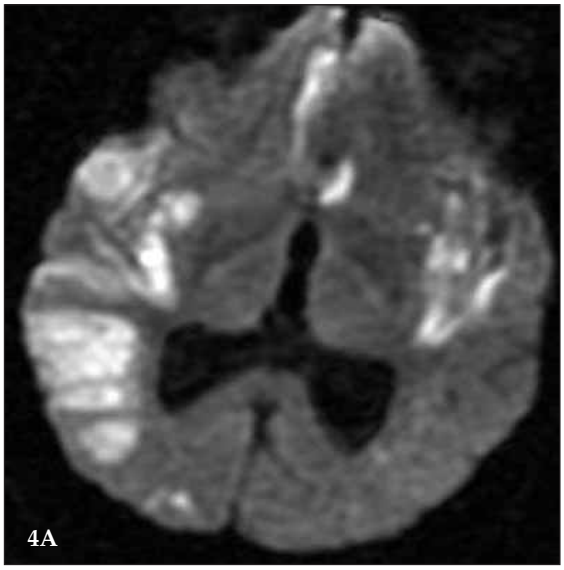


Figure 3: *Postoperative CT scan showing infarct occurring in region of restricted diffusion.*



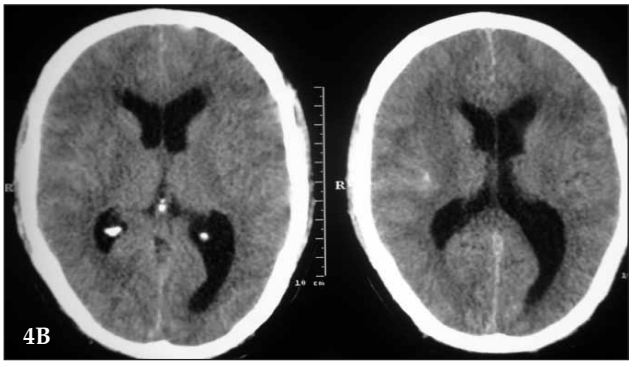


Figure 4: *Presence of extensive areas of restricted diffusion in preoperative DWI image (**A**) and absence of infarct in postoperative CT scan (**B**).*

was statistically significant ($p<0.05$) (Table 3). Angiographic vasospasm was seen in 4 patients (44.4%) with DWI abnormalities and in 2 patients (28.6%) without DWI abnormalities ($p>0.05$). 4 patients with DWI abnormalities showed hyperintensity on T2W images while none with a normal DWI showed abnormalities on T2W images (Table III).

It was observed at a follow up of 2 to 6 months that among 9 patients with restricted diffusion, 7 (77.8%) showed a poor clinical outcome ; and among 7 patients with no DWI abnormality, only 2 (28.6%) patients showed a poor clinical outcome.

DISCUSSION

Vasospasm occurs in about one-third of cases of aneurysmal subarachnoid haemorrhage as a response of intracranial arteries to the cisternal accumulation of blood. In approximately 10% of cases, the vasospasm becomes symptomatic with permanent neurological deficits related to cerebral infarct. The treatment of vasospasm is mainly preventive and requires nimodipine and hypertensive, hypervolemic and hemodilutional therapy. To be effective, this treatment must be started early and requires imaging investigations. A number of studies have shown the effectiveness of DWI in the early detection of cerebral ischemia. [1, 11, 14, 17, 20] DWI has a high sensitivity (88%-100%) and false positive lesions are rare. DWI changes have

Table III: Relation between DWI abnormalities and preoperative focal deficits.

DW1	Focaldeficit		T1W abnormality		T2W abnormality		Vasospasm (Angiographic)		Post.op CT (infarct)	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Restricted (n=9)	7	2	0	9	4	5	4	5	7	2
(%)	77.8	22.2	0	100.0	44.4	55.6	44.4	55.6	77.8	22.2
Not restricted (n=7)	0	7	0	7	0	7	2	5	1	6
(%)	0	100.0	0	100.0	0	100.0	28.6	71.4	14.3	85.7
P value	**<0.05(S)**		>0.05(NS)		>0.05(NS)		<0.05(NS)		**<0.05(S)**	

S-Statistically significant, NS-Statistically insignificant.

been reported in cerebral abscess and tumour where it occurs due to high viscosity in the former and attenuated cell packing in the latter. But when routine T1W,T2W and contrast studies are added, these lesions are easily differentiated.

Powers et al studied the mechanism of brain injury after subarachnoid hemorrhage using both MRI and positron emission tomography (PET). In early stage of ischemia there is reactionary cerebral vasodilatation leading to increased cerebral blood volume which ensures constant oxygen supply. In latter stages brain reacts by increasing oxygen extraction from cerebral blood. When oxygen extraction reaches its maximum the compensatory mechanisms fail and cerebral autoregulation is lost leading finally to cell dysfunction and death if ischemia continues.[19]

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.[9] DWI denotes the ischemic core, however in many studies abnormal regions on DWI did not progress to infarction.[12,13,14] These studies were mainly done in animals, but some studies in animals have also shown reversibility of DWI lesions. [3]

There are, however, only a few studies that have evaluated this technique during vasospasm following aneurysmal subarachnoid hemorrhage.[6, 10] A lesion showing restricted diffusion is strongly correlated with irreversible infarction. Reversibility of ischemic lesions on DWI has been identified in animal models showing both a time threshold and ADC threshold. [5, 2] In humans, there are a few reports showing reversibility of these lesions. [12]The lesions shown on DWI did not progress to infarction in two of our patients (Figure 4) with triple-H therapy and the patients had clinical improvement of deficits, although the documentation was with postoperative CT rather than MRI. Our work indicates that DWI may be used to show early brain damage in patients with vasospasm. The DWI changes were mainly confined to the cerebral cortex and were often more widespread than indicated by the location of aneurysm rupture in the anterior communicating artery territory. Moreover, DWI restriction was seen in many more patients than predicted by the preoperative angiogram.

DWI detects ischemic lesions within minutes after arterial occlusion. [18]ADC shows rapid decreases after ischemia due to cytotoxic edema and the taking up of water by the ischemic cells. [13] In chronic infarcts, however, there is an increase in ADC due to tissue necrosis leading to increased extracellular spaces and CSF in the area of the chronic infract. Kucharacayk et al., found that the decrease in ADC was not seen readily in partially reduced flow states. [7] This strongly suggests that when collateral blood flow is sufficient to prevent breakdown of the cellular metabolism, ADC does not drop. In contrast, T2W images detect vasogenic edema, the changes of which are apparent hours after the onset of ischemia. [13] Thus, it is less sensitive in the early detection of ischemic injury. In our study, among the patients who had developed an infarct in the postoperative period (those with a poor radiological outcome), 87.5% patients showed the presence of preoperative DWI abnormalities

while only 50% had T2W changes and none had CT scan abnormalities.

Most of our patients with a poor clinical grade had restricted diffusion. The greater amount of subarachnoid blood (represented by a higher Fischer grade) in these patients (Table1) may have been responsible for a greater degree of vasospasm and hence, a greater degree of abnormalities detectable in DWI

In the present study, the clinical outcome at follow-up was also related to the preoperative DWI changes. The patients with abnormalities on DWI scan appeared to fare far worse following intervention than did patients without such abnormalities. This fact may help in deciding when to intervene in impending ischemia due to vasospasm.

Only patients of anterior communicating artery aneurysm were chosen so that our results would not be affected by vasospasm in different territories depending on the site of aneurysm. Anterior communicating artery aneurysms formed the commonest aneurysms in our series and therefore provided the largest number of patients who could conform to our inclusion criteria. Since DWI is extremely sensitive in detecting acute ischemia, only those patients who were within 5 days of their ictus were included in the study.

CONCLUSION

DWI is effective in assessing the ischemic brain damage produced by vasospasm due to SAH. It can detect areas of ischemic injury much before CT scan can detect them or by TIW and T2W sequences of MRI and the abnormalities seen on DWI appear to bear a strong prognostic value.

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