Original Article

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Application of DWI in Evaluating Parenchymal Lesions of Cerebral Venous Thrombosis

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Abstract

Background: Cerebral venous thrombosis (CVT) is a potentially life-threatening emergency. It is a cause of stroke with inconspicuous patho physiological properties that differ from arterial stroke. Diffusion-weighted MRI (DWI) helps in differentiating arterial and venous strokes. **Objectives:** To study the pattern of diffusion weighted imaging with its evolution over time in patients with cerebral venous thrombosis **Subjects and Methods:** Fifty patients with clinical CVT underwent DWI, conventional MRI and MRV in Department of Radiology, JJM Medical College, Davangere. Apparent diffusion coefficient (ADC) values were measured in all of the abnormal lesions seen on DWI. **Results:** Four different DWI patterns were observed: 1) Hemorrhagic infarcts associated with heterogeneous signal intensity.2)Non-hemorrhagic infarcts demonstrating high signal intensities which were confirmed with ADC values atinitial and follow up studies. 3) No DWI changes with increased ADC values 4) Intraparenchymal hemorrhage showing decreased signal intensity on DWI with increased ADC values. **Conclusion:** The current study suggests that DWI with ADC values can be used to differentiate between vasogenic and cytotoxic oedema for tissue viability, early detection of ischemia and also helps in assessing the severity and prognosis of parenchymal changes in patients with CVT.

Keywords: cerebral venous thrombosis; magnetic resonance imaging; diffusion weighted imaging; apparent diffusion coefficient.

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Introduction

Cerebral venous thrombosis (CVT) or Dural sinus venous thrombosis (DSVT) is a relatively uncommon neurologic disorder that is potentially reversible.[1] Duralsinus thrombosis, combined with thrombosis of the deep or cortical cerebral venous system and resulting venous stroke is more common than once thought.[2] CVT occurs in three to four per 1 million individuals in the general population.[3] The pathogenesis is multifactorial and the disease may occur at any age which is often associated with nonspecific symptoms.[1] The first clinical presentation is variable and ranges from headache, raised intracranial pressure to severe multifocal deficits, seizures, and coma.[4] Cerebral venous thrombosis (CVT) is potentially serious and life-threatening cause of stroke, accounting for 0.5–1% of all strokes.[1] The pathophysiology is increased pressure in superior sagittal sinus resulting in reduced capillary perfusion pressure, increased cerebral blood volume, obstruction of venous flow leading to increased intracranial pressure and blood–brain barrier disruption, resulting in decreased cerebral blood flow, increase in net capillary filtration, leading to progressive cerebral oedema, and intracerebral and subarachnoid hemorrhage additionally compromising the brain tissue and the coexistence of cytotoxic and vasogenic oedema.[4]

Acute arterial strokes show cytotoxic oedema, whereas venous strokes are thought to contain vasogenic and interstitial oedema due to venous congestion. The underlying risk factors and clinical manifestations of CVT are highly diverse which make early diagnosis much difficult, however neuro imaging plays a key role in the diagnosis and further treatment. The structural imaging head computed tomography (CT) and routine brain magnetic resonance imaging (MRI)] can assess any parenchymal lesion secondary to the venous thrombosis and reveal direct signs of Intraluminal thrombus with the latter being more superior.[5] However conventional MRI cannot differentiate between vasogenic oedema and cytotoxic oedema.[6]

Some special MRI sequences, such as Diffusion weighted imaging(DWI), relatively new MRI technique based on the molecular motion of water, is sensitive in detecting strokes due to Cytotoxic and vasogenic oedema.[4]DWI is one of the quickest MRI sequences to obtain, which can be used in the diagnosis, characterization and follow-up of a variety of pathologies outside the brain parenchyma. Some important diagnoses, such as dural sinus thrombosis, empyema and ventriculitis can potentially be overlooked on other sequences but are more conspicuous on DWI, as they “stand out” against a dark background on the high b-value images. This new fast neuro imaging technique will give insight to

the patho physiological mechanism as well as prognosis of CVT.[7] This study looks at the application of diffusion-weighted MRI technique in cerebral venous thrombosis.

Subjects and Methods

Source of Data

A hospital based cross sectional descriptive study was conducted with a calculated sample size of 50 patients over a period of 2 years from October 2017 to September 2019, who had clinical signs and symptoms of cerebral venous thrombosis and referred to Department of Radiology, JJM Medical College, Davangere.

Claustrophobic patients and patients with MRI incompatible implants were excluded from the study.

$$\text{Sample Size} = \frac{Z\alpha^2}{d^2} P(1-P)$$

$Z\alpha^2$= Std normal variant 1.96
P = Expected proportion from population

d = Absolute error
Eg: Prevalence of CVT in India = 0.5%,

With 5% error sample needed is 08 cases
Minimum of 8 cases maximum of 50 cases has been selected to conduct this study

Data Collection

After obtaining a written informed consent a detailed history was taken and clinical examination was done. The findings were tabulated. Then the patients were evaluated by 1.5 tesla Philips (Achieva) MRI machine with the patients in supine position.

Patients had undergone diffusion weighted imaging along with conventional MRI and MR Venogram. The diagnosis of CVT was confirmed with MR Venogram and other conventional MR sequences in all the patients.

Diffusion weighted images with echo planar imaging were obtained using two b values (0 and 1000).

MR Venogram was done using TOF (time of flight) technique in oblique Sagittal and coronal planes. The follow up MRI imaging were done at 1 month and 3 months of initial presentations.

The region of interest (ROI) was chosen on the abnormal intensity area, avoiding hematoma on T2 weighted or diffusion weighted images, in order to calculate ADC values. The areas with maximum and minimum ADC are taken as the representative lesions when multiple areas of abnormal intensity were observed. In follow up studies with diffusion-weighted imaging, and ROI was placed on the same areas used in the initial study.

Statistical Analysis

Categorical data is represented in the form of frequency and percentage. Quantitative data was represented using mean & Standard deviation. Analysis of quantitative data between two groups was done using unpaired t test if data passes 'Normality test'. Comparison of mean within the group was done with paired t test. A P value of <0.05 was considered statistically significant.IBM SPSS Version 22 for windows was used for analyzing the data.

Results

Image analyses of 50 patients (16 males and 34 females)[**Graph-1**] with an age range of 4 days to 55 years and a mean age of 26.33 years was done

Common clinical presentations in the decreasing order were headache (74%), seizures and giddiness (54%) each, vomiting (50%), neurological defect and altered sensorium (40%) each, fever (38%), blurring of vision (30%), and loss of consciousness (20%).

Delay between clinical onset and 1st MRI investigation ranged from 1-3days. With most of the cases being Imaged on day 1 (46%).[**Graph-2**]

Of 50 patients, 18 had hemorrhagic infarcts, while 9 had non-hemorrhagic infarcts, 8 had intra-parenchymal hemorrhage and 15 had no parenchymal changes on DWI images.[**Graph-3**]

In all cases, cerebral venous infarctions were identified on conventional MR images, with no patient showing hyperintensity on diffusion weighted images in the absence of conventional MR findings.

The normal ADC values (+/- 2SD) of the control areas (unaffected side of brain) in 50 patients were 0.73- 0.95 x $10^{-3}mm^2$/sec.

In the hemorrhagic infarcts patients, diffusion weighted images showed heterogeneous signal intensity with dark low signal intensity areas corresponding to hemorrhage while the bright regions represent the infarcted brain. The ADC maps depicted decreased values($0.63 \pm 0.36 \times 1000^{-3}$sqmm/s)in the region of very bright signal intensity, while the hemorrhagic regions showed variable ADC values on DWI [**Table-1**] [**Figure-1**]

In cases of non-hemorrhagic infarcts, focal or multifocal areas of high signal intensity in DWI were noted. The ADC values at the region of high signal was found to be lesser than the normal brain parenchyma ranging from 0.30-0.69 $x1000^{-3}$sqmm/s at the time of initial imaging with the mean ADC value found to be $0.59 \pm 0.10 \times 1000^{-3}$sqmm/s [**Table-2**] [**Figure-3**]

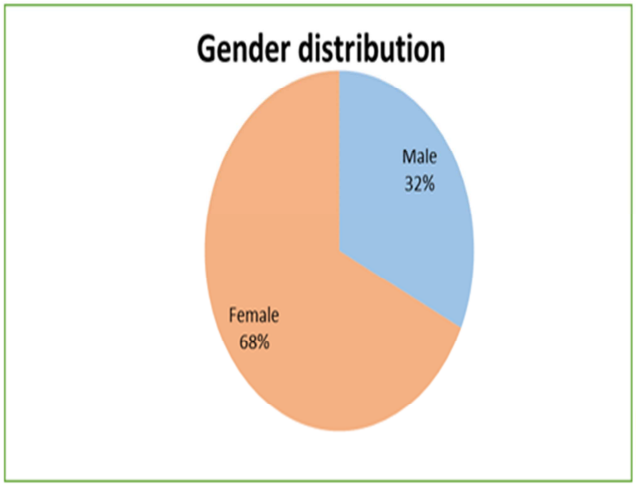
In cases of intra-parenchymal hemorrhage the DWI images showed areas of decreased signal intensity corresponding to hemorrhage. ADC values were predominantly on the higher side.[**Figure-2**]

Subarachnoid hemorrhage along with hemorrhagic infarct was seen in 1 case which had involvement of superior sagittal sinus, bilateral transverse & sigmoid sinuses with cortical veins and deep venous system

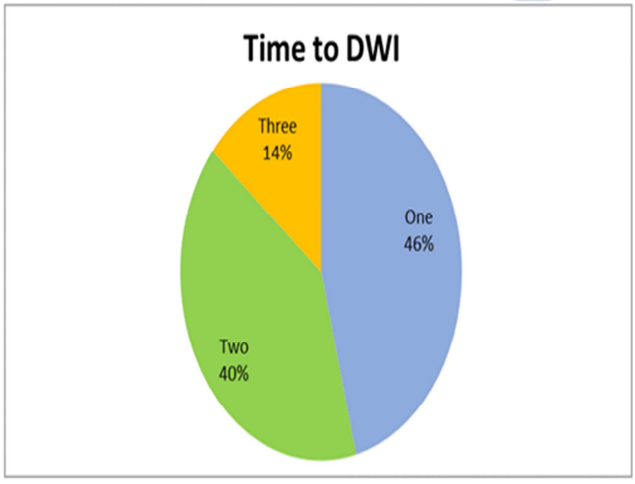
Among the 15 cases of no parenchymal changes in DWI, 8 cases showed parenchymal hyper intensities in conventional sequences with no true restriction on DWI and no blooming on gradient sequence. ADC values were on the higher side with a mean value of $1.92 \pm 0.07 \times 1000^{-3}$sqmm/s suggesting the possibility of vasogenic oedema. Rest of the 7 cases had no parenchymal changes either in DWI or in conventional sequences and these cases were studied on day one of symptoms.

Repeat MRIs were performed in 27 cases to assess the time course of diffusion changes. In subsequent scans done after one month, all the areas with decreased ADC in non-

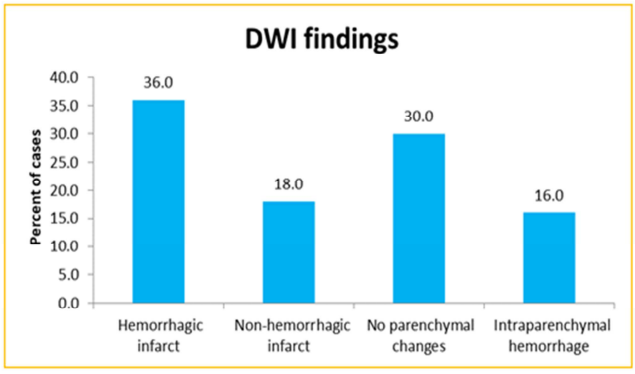
hemorrhagic infarcts on the earlier scans showed reduction of parenchymal hyperintensities. Further scan done after 3 months showed a near complete resolution of the signal abnormalities on both T2W and DWI images which were correlated with ADC values. Hemorrhagic infarcts on the other hand did not show significant improvement in ADC at 1 month of scan but however showed improvement at 3 months of study.[**Graph4**].



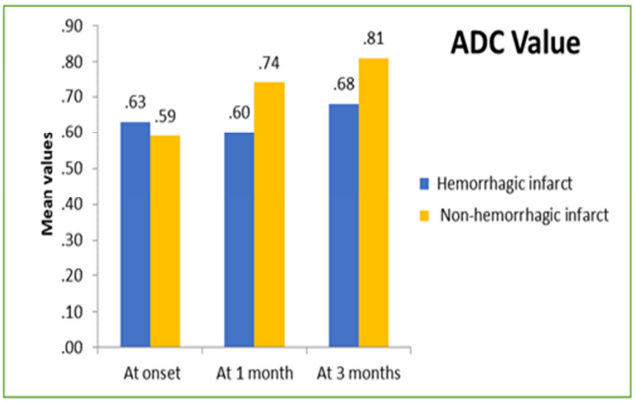
Graph 1: Gender distribution of cases with cerebral venous thrombosis



Graph 2: Day of imaging in CVT patients



Graph 3: Parenchymal changes in patients with CVT



Graph 4: Time course evaluation of diffusion changes

Table 1: Mean ADC values of haemorrhagic infarct at 0, 1 and 3 months interval

ADC value (x1/1000 sqmm/s) in Hemorrhagic infarct				
Groups compared	Mean difference	Std. Deviation	Paired t test	
			P Value	Significance
At onset Vs At 1 month	.03	.56	0.848	NS
At onset Vs At 3 month	-.06	.59	0.69	NS
At 1 month Vs At 3 months	-.08	.06	0.001	HS
NS= Not Significant, HS= Highly Significant				

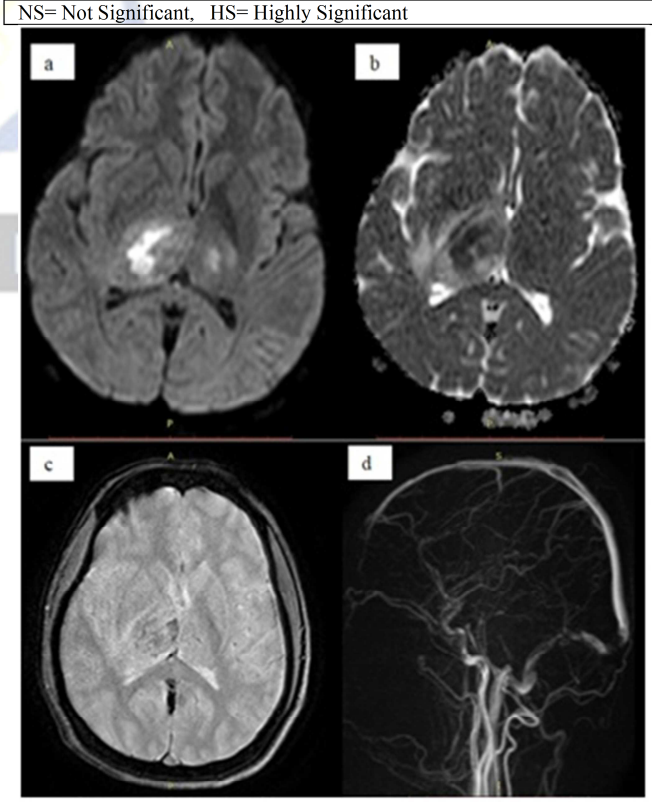


Figure 1: A case of postpartum day 3 presented with headache and seizures showing true restriction on DWI (a) with corresponding ADC (b) matching and areas of blooming on gradient sequence (c) in right thalamus. TOF MRV (d) showing thrombosis of straight sinus, internal cerebral veins, confluence of sinus, left transverse, left sigmoid and left internal jugular veins

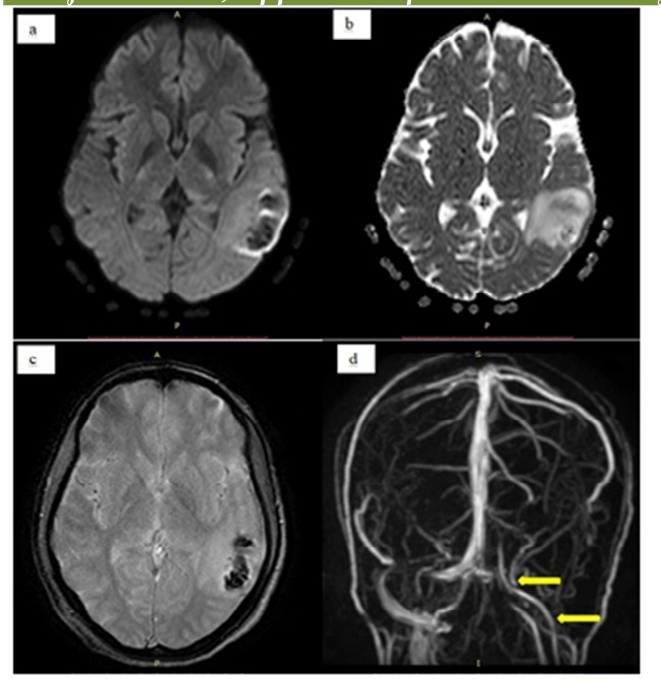


Figure 2: Adult male presented with headache and weakness showing altered signal intensity on DWI(a) and ADC(b) with no true restriction and shows areas of blooming on gradient sequence(c) in left temporal lobe. TOF MRV(d) showing thrombosis ofleft transverse,left sigmoid and left internal jugular veins.

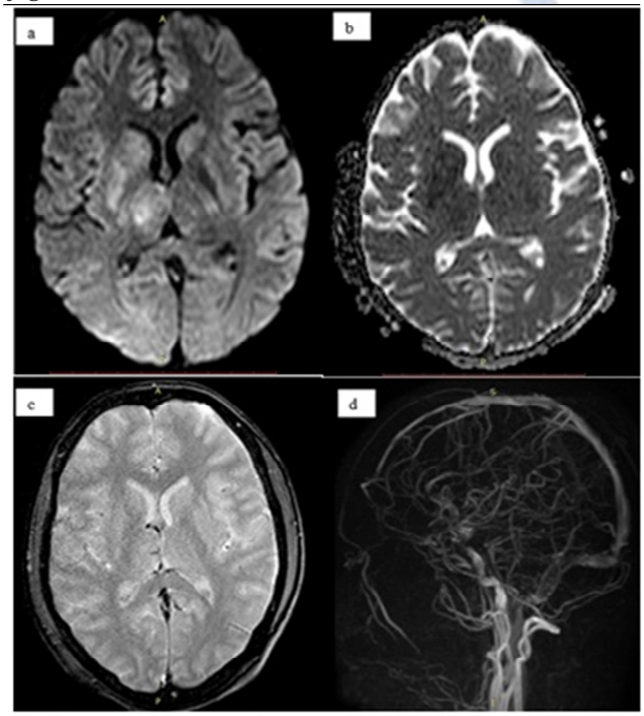


Figure 3: A 32years old female patient demonstrating multifocal DWI (a) high signal intensities involving right caudate, lentiform nucleus and right thalamus which are showing corresponding restriction on ADC (b) and no blooming on gradient sequence (c). Sagittal TOF MRV (d) showing thrombosis of internal cerebral veins, vein of Galen, straight sinus, left transverse sinus, sigmoid sinus and extending into left IJV

Table 2: Mean ADC values of non-haemorrhagic infarct at 0, 1 and 3 months interval

ADC value (x1/1000 sqmm/s) in Non-Hemorrhagic infarct				
Groups compared	Mean difference	Std. Deviation	Paired t test	
			P Value	Significance
At onset Vs At 1 month	-.15	.03	0.000	HS
At onset Vs At 3 month	-.22	.06	0.000	HS
At 1 month Vs At 3 months	-.07	.04	0.001	HS
HS= Highly Significant				

Discussion

Dural sinus thrombosis, along with thrombosis of the deep or cortical cerebral venous system and subsequent venous stroke is more common than once thought. Cerebral venous thrombosis (CVT) is a cause of stroke with varied etiologies and diverse clinical presentations. Its appearance may mimic acute arterial strokes or a mass lesion, thus radiological examinations plays a vital role in the diagnosis of CVT and helps to predict the prognosis. MRI and MR Veno graphy are useful methods to establish the diagnosis.

Conventional MR imaging (T2andFLAIR) showed similarly high signal intensities for the areas of venous congestion and infarct, and cannot differentiate between Cytotoxic and vasogenic oedema. Diffusion weighted imaging provides ADCs that can distinguish whether the associated cerebral oedema is of cytotoxic origin or vasogenic oedema. However, the findings on diffusion weighted imaging and the ADC value changes in relation to the disease progression in patients with dural sinus thrombosis remains to be explained.

Various patterns have been observed in the DWI findings:

Heterogeneous SI of hemorrhagic venous infarct and low signal intensity in intraparenchymal hemorrhage

Parenchymal hemorrhagic infarcts were seen in 18 patients with cerebral venous thrombosis. The patho physiology of hemorrhage is multi factorial. Hemorrhage may be caused by continued arterial perfusion in areas of cell death, as can be seen at reperfusion in arterial Ischemia. Elevation of venous pressure beyond the limit of the venous wall was also thought as the cause.[8]

Heterogeneous SI group on diffusion weighted imaging included hemorrhagic venous infarctions. The Signal intensities were credited to hemorrhage. The bright signal intensity of the hemorrhagic clot on DWI was due to the paramagnetic effect of the intracellular met-hemoglobin, and the surrounding low SI with high ADC values was due to vasogenic oedema. Between these, a thin rim of low signal was observed, suggesting the occurrence of hemosiderin. These findings were similar to the findings reported by kon Chu et al[9]

Diffusion weighted imaging and ADC measurement of intra cranial hematoma were recently reported by Atlas et al[10], but in our study ADC values of hematoma were avoided. The reason being, the determining factors of ADC values in hematoma may be due to paramagnetic effects of met-hemoglobin rather than true restriction of water movement.

High SI of Non-Hemorrhagic Venous Stroke

These presentations were seen in 9 patients. The findings were focal and multifocal high signal intensities in DWI. In all patients, the ADC values were low (ADC) as seen in arterial stroke. Time interval from onset to DWI was variable (ranging from one to three days). DWI findings of this group may signify the acute stages**.**

Forbes et al[11] stated the initial ADC decrease in patients with CVT and the ADC decrease returned to normal or increased within 4 days**.**

Kon Chu et al[9] also described similar findings, followed by which anti coagulation was immediately initiated and the clinical symptoms disappeared completely after the anti coagulation therapy. Yet, the clinical relevance of this pattern is uncertain.

The patho physiological process behind this pattern may represent cytotoxic oedema due to congestive ischemia in regions with adequate venous collaterals. According to Kon Chu et al, clinical deficits in these patients did not match the lesions, suggesting that DWI may not be sensitive to the pathophysiological processes in these patients.

Detection of early venous infarct In our study, all cases of cerebral venous infarct demonstrating hyperintensity on diffusion weighted images also showed T2 signal changes. This is probably explained by image timing, because we did not image any subjects hyper-acutely, when diffusion restriction might have been present in the absence of T2 hyperintensity. This also explains the time from on set of disease to DWI was variable and non-uniform. This can be accredited to varied linical manifestations of CVT.

Time course of diffusion lesion evolution

In the present study, we showed the ADC changes and its relevance with the time course in patients with dural sinus thrombosis. The results demonstrated that vasogenic oedema develops more often and earlier in dural sinus thrombosis, though both vasogenic and cytotoxic oedema are associated with the pathological condition in the early phase of the disease.

The influence of vasogenic oedema is dominant in the early phase of dural sinus thrombosis. In our study 8 cases showed increased ADC values (mean ADC of $1.92x10^{-3}$sqmm/sec) with no true diffusion restriction.

Increase in ADC advocates prevalence of vasogenic oedema in the early phase of the CVT. It was stated that the reduction in ADC persisted up to 6 days, on average after stroke, due to arterial ischemia and that a substantial reduction of ADC was detected for atleast 4days. ADC changes in the early phase of dural sinus thrombosis differ from those of arterial ischemia, in which cytotoxic oedema is prime in the hyperacute or acute phase (2, 9).

Conclusion

In the present study, we showed the initial diffusion weighted patterns with ADC changes and its association with the time course of diffusion lesion evolution in cerebral venous thrombosis. The results specify, both vasogenic and cytotoxic oedema are related to the pathological condition in the early phase of CVT. Our report demonstrated the coexistence of increased and decreased ADCs in hemorrhagic infarcts. Increase in ADC suggests high proportion of vasogenic oedema and decrease in ADC suggests cytotoxic oedema. Based on our results, decrease of ADC, supposed to represent more severe pathological conditions and residual neurologic deficit and they are the last areas where signal intensity reverse back to normal values.

The limitation of this study was we did not image any of the patients in hyper acute stage, so DWI played no role in recognition of hyperacute stroke in CVT.

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