Cerebral Venous Thrombosis: Diagnosing Accuracy of Magnetic Resonance Imaging Brain and Magnetic Resonance Venography

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ABSTRACT

Background

Cerebral venous thrombosis (CVT) potentially reversible, a relatively rare neurologic condition. It denotes cerebral venous thrombosis-induced intraluminal blockage. The gold standard in the investigation is now magnetic resonance venography (MRV) with magnetic resonance imaging (MRI) to accurately diagnose CVT.

Objectives

1. To evaluate the CVT using T1W, T2W, FLAIR, DWI and MRV.
2. To study the pattern of distribution of superficial and deep CVT on MRV.
3. To study the parenchymal abnormalities associated with CVT.

Methods

This study comprised 50 patients from the hospitals affiliated with Mysore Medical College and Research Institute who were diagnosed with CVT on MRI and MRV between November 2018 and August 2020. Using a 1.5TMRI 8 channel GE BRIVO MRI machine, each patients were evaluated.

Results

Puerperium was the most frequent risk factor in our study, with a considerable female preponderance and a common age group of 21–30 years old. Headache was the most frequent symptom, followed by seizures. The most often affected sinus was the SSS. About three-quarters of the patients had focal parenchymal abnormalities. Most frequently seen focal parenchymal abnormality was hemorrhagic infarct. Focal parenchymal abnormalities were categorised as either cytotoxic or vasogenic oedema using DWI, with the former being more prevalent. In every patient evaluated in our study, MRV revealed

thrombosis. T1/T2WI detected CVT in 79.2% of the thrombosed venous segments. T2* detected all the superficial cortical vein thrombosis and thrombosed deep venous segments detected on MRV.

Conclusion

MRV in combination with MRI is the most comprehensive, non-invasive, safe, in-vivo diagnostic modality for delineation of venous anatomy, diagnosis of cerebral venous thrombosis and its extent of involvement, parenchymal involvement, predicting the prognosis and follow-up.

Keywords: CVT, MR VENOGRAPHY, MR

DOI Number: 10.48047/nq.2024.22.1.NQ24047 **NeuroQuantology 2024; 22(1):525-535**

INTRODUCTION

Cerebral venous thrombosis (CVT) or Dural sinus venous thrombosis (DSVT) is a relatively uncommon neurologic disorder that is potentially reversible.[1] It means intraluminal obstruction by cerebral venous thrombosis (CVT) or external compression.

Over the last decade, magnetic resonance imaging (MRI) is an effective alternative to this method and with the use of MR Venographic (MRV) techniques, is fast becoming one of the modalities of choice for diagnosis and evaluation of dural sinus and cerebral venous thrombosis wherever MRI facility is available.[2]

Some special MRI sequences, such as diffusion-weighted imaging (DWI), a relatively new MRI technique based on the molecular motion of water, are sensitive to detecting strokes due to cytotoxic and vasogenic oedema.

TOF MR Venography is the most commonly used method for the diagnosis of cerebral venous thrombosis.[3]

The combination of MRI and MRV allows for an accurate diagnosis of CVT and is now the gold standard in the investigation of this disease.[4]

AIMS AND OBJECTIVES

1. To evaluate the findings of cerebral venous sinus thrombosis (CVT) using T1W, T2W, FLAIR, Diffusion-weighted images and Magnetic resonance venography (MRV).
2. To study the pattern of distribution of superficial and deep cerebral venous thrombosis on Magnetic Resonance Venography.
3. To study the parenchymal changes associated with cerebral venous thrombosis.

MATERIALS AND METHODS

This is a descriptive study conducted among 50 patients who were found to have CVT on MRI and MRV in the hospitals attached to Mysore Medical College and Research Institute, Mysore from November 2018 to August 2020. After obtaining written consent from the patients, a detailed history along with a complete clinical examination and laboratory investigations were done before the MRI examination.

Sample Size Calculation

The sample size was calculated using the formula n=z2pq/d2, the calculation was based on the prevalence of cerebral venous thrombosis as evaluated by MRI which is equal to 2.5%, with allowable absolute error considered as 6% and standard normal variant for 6% alpha error, which is 4%. The sample size was determined to be 50. Purposive sampling was done.

Inclusion Criteria

1. All patients were confirmed by MRI &MRV as having cerebral venous sinus thrombosis.
2. All age groups and both sexes were included.

Exclusion Criteria

1. Patients having a history of claustrophobia
2. Patients with a history of metallic implant insertion, cardiac pacemakers and metallic foreign body in situ.

3. Patients who were not willing to give consent.

Statistical Methods Applied

Descriptive statistics, crosstabs (Contingency table analysis) and chi-square test were used. The descriptive procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which you select the variables (the default). The crosstabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. The chi-square test procedure tabulates a variable into categories and computes a chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values. All the statistical calculations were done through SPSS for windows (v 16.0).

Imaging Protocol Used

All patients were evaluated with a 1.5T MRI 8 channel GE BRIVO MRI Machine. Sequences used were Axial T1 SE, Sagittal T1 FLAIR, Axial and Coronal T2FSE, Axial FLAIR, Axial T2* and 2DTOF. The 2-dimensional time of flight (2DTOF) sequence was done in the sagittal plane and then the source images were reconstructed into three-dimensional maximum intensity projection (3D MIP) images.

RESULTS

In the present study, there was a slight female preponderance with 54 % of the patients being them. In the present study, the commonest age group was found to be between 21-30 yrs of age with 34 % of patients falling in this age group. This was followed by 31- 40 yrs of age with 26% of patients falling in this age group.

The mean age of the patients was found to be 36.1 years, with the mean age of the female patients being 34.8 years whereas the mean age of the male patients was 37.7 years.

In the present study, the cause for CVT couldn‘t be found in 22% of cases. Among the cases in which the cause for CVT was found, puerperium (26%) was the commonest one. It was followed by alcohol consumption (16%), dehydration (14%) and sepsis (10%).

In the present study, headache (68%) was the most common symptom, followed by seizures in 40% of cases.

In the present study, focal brain abnormalities were found in 74 % of the cases. The most common focal brain abnormality was a haemorrhagic infarction found in 54 % of cases followed by non-haemorrhagic infarction in 20 % of cases.

In the present study with the help of diffusion-weighted imaging, the focal abnormalities were categorized as coexistent vasogenic and cytotoxic oedema in 40% of cases, purely vasogenic oedema in 30 % of cases and purely cytotoxic oedema in 4 % cases.

In the present study, the focal parenchymal changes were found to be bilateral in 22 % of cases, right-sided in 20 % of cases and left-sided in 32% of cases.

	No. of Cases	**Percentage**
RT Frontal	16	32%
LT Frontal	16	32%
RT Parietal	8	16%
LT Parietal	15	30%
RT Temporal	5	10%
LT Temporal	5	10%

RT Occipital	3	6%
LT Occipital	3	6%
Basal Ganglia	2	4%
Thalamus	1	2%
Brain Stem	3	6%
Cerebellar Hemisphere	3	6%
Table 1. Distribution of Patients with CVT Depending on the Lobe Involved		

Sinuses Involved	**Number of Patients**	**Percentage**
Superior Sagittal	34	68%
Right Transverse	19	38%
Right Sigmoid	13	26%
Left Transverse	21	42%
Left Sigmoid	17	34%
Straight Sinus	8	16%
Vein of Galen	2	4%
Internal Cerebral Vein	4	8%
Basal Vein of Rosenthal	2	4%
Cortical Veins	14	28%
Cerebellar Veins	2	4%
Distribution of patients with CVT depending on the sinuses involved		
SAH	**Number of Subjects**	**Percentage**
Present	7	14%
Absent	43	86%
Total	50	100%
Distribution of patients with CVT depending on the presence of SAH		
Table 2		

In the present study, the most common sinus to be affected was the superior sagittal sinus (68% cases), followed by the left transverse sinus (42% cases), right transverse sinus (38 % cases), left sigmoid sinus (34 % cases), right sigmoid sinus (26% cases) and straight sinus (16 % cases).
In the present study, sub arachnoid haemorrhage was found in 14 % of the cases with CVT.

	Number of Cases	**%**	**Chi- Square**	**P value**
Detected by MRV	50	100.0	0.017	0.896
Detected by T1 and T2	48	96		
Distribution of patients with CVT depending on detection by MRV and T1/T2 weighted sequences				
	No. of Venous Segments	**%**	**Chi Square**	**P Value**
Detected by MRV	120	100%	1.744	.187
Detected by T1/T2	95	79.2%		

Detection of thrombosed venous segments confirmed with MRV by T1/T2 weighted sequences				
	Number of Patients with Cortical	**%**	**Chi Square**	**P Value**
	Venous Thrombosis			
Detected by T2*	15	100%	1.923	.166
Detected by T1/T2	7	46.6%		
Detection of cortical venous thrombosis with T2* and T1/T2 Sequences				
Table 3				

A chi-square value of 0.017 and probability value of 0.896 reveal a non-significant difference between MRV diagnosis and T1 and T2 diagnosis in many patients with CVT.
The chi-square value of 1.744 and probability value of 0.187 reveal a non-significant difference between MRV diagnosis and T1 and T2 diagnosis of the extent of thrombosis of venous segments in patients with CVT. A chi-square value of 1.923 and probability value of 0.166 reveal a non-significant difference between T2* diagnosis and T1 and T2 diagnosis of a number of patients with cortical venous thrombosis.

	No of Thrombosed Deep Venous Segments	**%**	**MRV&T1T2**		**MRV&T2***		**T2* &T1T2**	
			X^2	**p**	**X^2**	**p**	**X^2**	**p**
Detected on MRV	15	100.0	6.400	.011	.000	1.000	6.400	.011
Detected by T2*	15	100.0						
Detected by T1&T2	2	13.3						
Table 4. Detection of thrombosed deep venous segments with MRV, T2* AND T1/T2 sequences								

A chi-square value of 6.400 and probability value of 0.011 reveal a significant difference between T2* diagnosis and T1 and T2 diagnosis of the extent of thrombosis in the deep venous system.
Similarly, a significant difference between MRV diagnosis and T1 and T2 diagnosis of the extent of thrombosis of the deep venous system was noted.

Representative Images

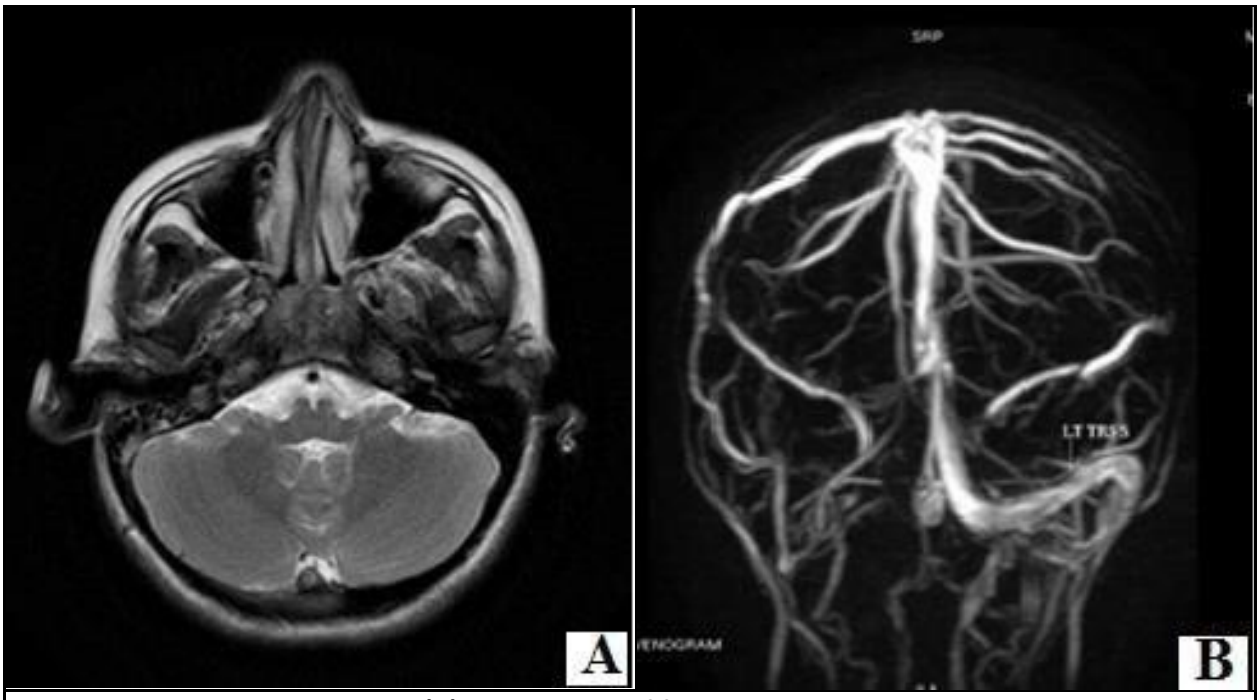
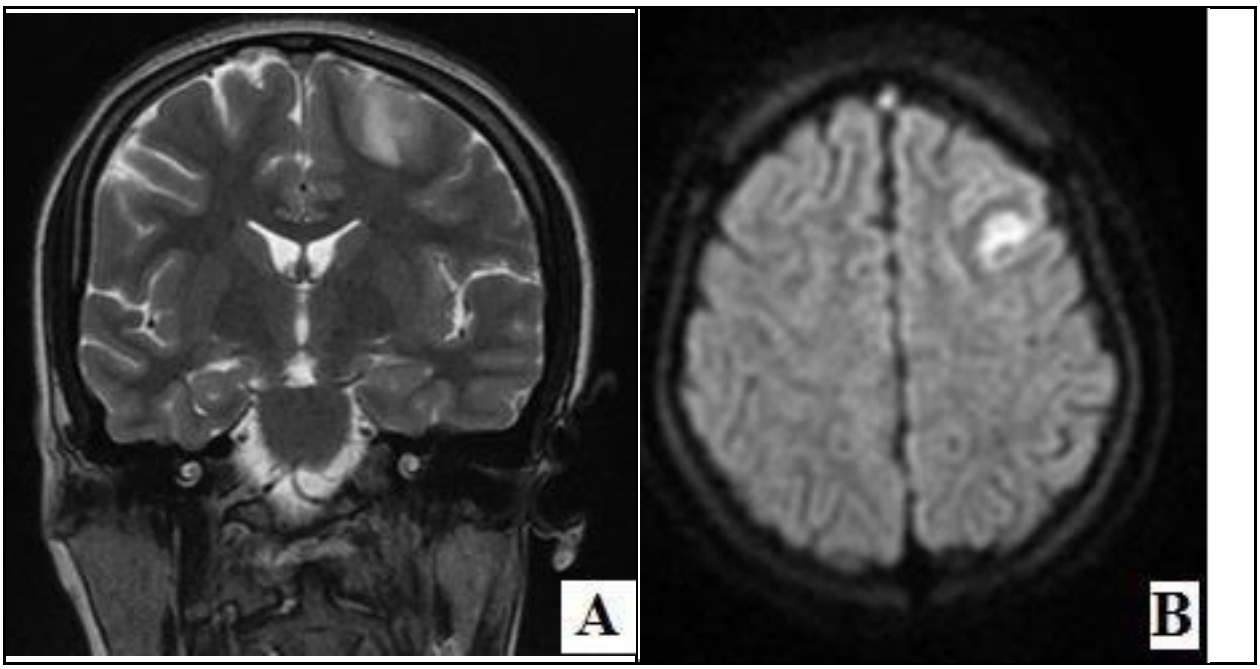


Image 1- Case 4: Axial T2W image (A) showing loss of flow void in right transverse and sigmoid sinuses with absence of flow in the same seen in 2DTOF MIP image (B) suggestive of thrombosis.



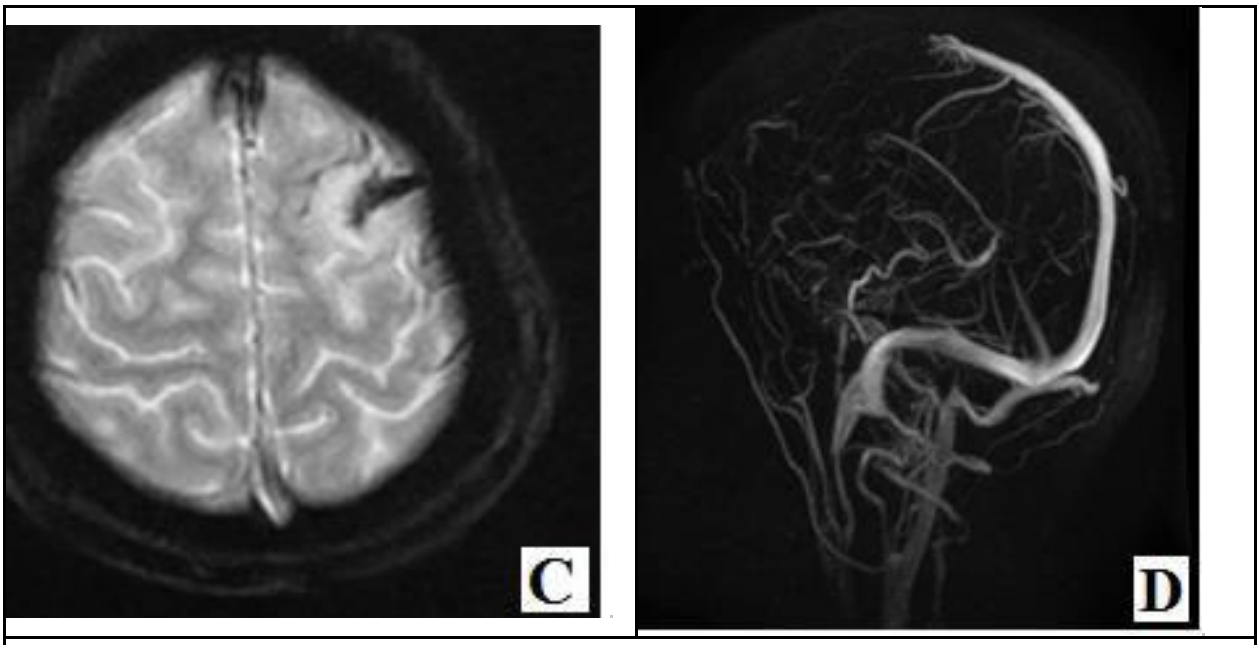


Image 2- Representative Case: Coronal T2W and DWI images showing loss of flow void in superior sagittal sinus, acute infarct in left frontal lobe. Axial T2* image showing blooming artifacts indicating hemorrhagic infarct. 2DTOF MIP image showing absence of flow in the anterior half of superior sagittal sinus.

DISCUSSION

The results of the present study agreed with Ameri and Bousser, who carried out extensive research; in 20 to 25 percent of cases, they found no cause. 7 According to Nagaraj et al,[5] the most common predisposing factor was puerperium, which they found in 200 out of 230 cases (86%) of CVT.

In his study of 110 cases, Bousser et al,[6] stated that cerebral venous occlusion in all patients was due to thrombosis.

In the study conducted by EmanAbd-El Latif et al., intraluminal thrombus was the most common cause of cerebral venous occlusion, occurring in 86.7 percent of patients.

Occlusion by external compression was seen in 13.3% and was caused by meningioma. In the present study, CVT due to intraluminal thrombus was seen in 94 % of the cases with 3 cases (6%) being caused due to external compression by malignancy.

This is different from Jeffrey et al.[7]who reported in his study that compression or invasion of cerebral sinuses from dural or calvarial metastases was the main cause in those patients with cerebral sinus occlusion due to solid tumours.

In a Dutch European study, the most frequent symptoms and signs were headache (38%), focal seizures with or without secondary generalization (34%) and paresis (unilateral or bilateral) in 30%.[8]

In a study done by Poon et al, they found that headache (75%) was the most common symptom followed by seizures (37%) and motor/ sensory deficit (34%).[9]

This was in line with the present study in which headache (68%) was the most common symptom, followed by seizures in 40% of cases and sensory changes in 26% of cases.

In about 50 percent of cases, focal changes

occur. The location of the parenchymal changes may not correspond to the sinus site involved.[10]

In 74 percent of the cases of the present study, focal brain abnormalities were observed. The focal parenchymal changes were found to be bilateral in 22 % of cases, right-sided in 20 % of cases and left-sided in 32% of cases, with the frontal lobe being the most commonly affected lobe.
Simonds et al.[11] observed focal oedema in 25% of cases, followed by non- hemorrhagic infarction in (40%) and hemorrhagic infarction in (26.7%). Nagaraj et al. found hemorrhagic infarction in (40.9%) and non-hemorrhagic infarction in (51.6%) of cases.

The most common focal brain abnormality in the present study was haemorrhagic infarction found in 54 percent of cases, followed by 20 percent of cases of non-haemorrhagic infarction. Parenchymal changes may be secondary to cytotoxic oedema, vasogenic oedema, or intracranial haemorrhage. Vasogenic and cytotoxic oedema patterns may coexist.

Haemorrhages may occur with both types of oedema, and various patterns may coexist in the same region.[12,13] The use of the term venous infarct in reference to these lesions should be discouraged given the variable nature of the parenchymal abnormalities that may occur in cerebral venous thrombosis since that term implies irreversibility.

Diffusion-weighted (DW) MR images can distinguish between vasogenic and cytotoxic oedema, unlike conventional MR images.

In a study done by Mullins et al 82, 13 patients with CVT were evaluated with DW imaging. Three lesion types were disclosed: lesions with elevated diffusion that resolved, consistent with vasogenic oedema; lesions with low diffusion that persisted, consistent with cytotoxic oedema in patients without seizure activity; and lesions with low diffusion that resolved in patients with seizure activity.

The focal abnormalities were classified as vasogenic oedema and cytotoxic oedema in the present study using diffusion-weighted imaging. Co-existing vasogenic and cytotoxic oedema was observed in 40% of cases, exclusively vasogenic oedema in 30% of cases, and exclusively cytotoxic oedema in 4% of cases. However, the cases were not followed up to see whether the diffusion restriction was due to cytotoxic oedema, which persisted or not.

Based on the results of the largest cohort ever published (624 patients), collected over a short period, cerebral venous thrombosis involved the following vessels in decreasing frequency: the superior sagittal sinus (62%), left and right transverse sinus (respectively 44.7% and 41.2%), straight sinus (18%), cortical veins (17.1%), deep venous system (10.9%), cavernous sinus (1.3%), and cerebellar veins (0.3%).[14]

This agreed with the present study in which the most common sinus to be affected was the superior sagittal sinus (68% cases), followed by the left transverse sinus (42% cases), right transverse sinus (38% cases), left sigmoid sinus (34 % cases), right sigmoid sinus (26% cases) and the straight sinus (16% cases). The vein of Galen (4%), internal cerebral veins (8%), the basal vein of Rosenthal (4%) and cerebellar veins were involved in (4%) of cases.
The superficial cortical veins were involved in 28% of cases. 3 cases of isolated involvement of the superficial cortical veins were observed.

Cerebral venous thrombosis (CVT)-related subarachnoid haemorrhage (SAH) is rarely mentioned in the literature. The exact cause of CVT-related SAH is unknown. Venous hemorrhagic infarct may be responsible for secondary rupture into subarachnoid spaces and trigger SAH. Dural sinus thrombosis with

secondary venous hypertension may lead to the rupture of weak, thin-walled cortical veins, leading to SAH in the subarachnoid space.[15]

However, 7 patients (14 %) were found to have a subarachnoid haemorrhage in the current study. Both cases had concomitant haemorrhagic parenchymal infarctions.
The combination of MRI and MRV helps CVT to be correctly diagnosed and is now the gold standard in the study of this disease.

In a study conducted by Vogl et al, they found that MR angiography is the technique of choice for diagnostic evaluation and follow-up of dural sinus thrombosis, and it is reliable as the sole examination for this condition.

Flowing blood usually creates a signal void with spin-echo sequences; stationary blood on the thrombus has been observed to produce higher signal intensity. This phenomenon is not entirely reliable; however, as a variety of flow-related artifacts can occasionally give rise to increased intraluminal flow signals that can mimic thrombus. Time-of-flight MR angiography, with its short repetition times and adjustable flip angles, allows the representation of flowing blood as areas of high signal intensity in contrast to a dark background of suppressed signals from stationary tissues.
For the detection of CVT, spin-echo MR images yielded variable results, showing some degree of dependence on the age of the thrombus. However, particularly in the case of a relatively acute thrombus, signal intensities were inconsistent and it was not possible to distinguish unequivocally between cessation of flow and low or normal flow.

The replacement of the normal flow void with an abnormal signal on T1/T2 weighted images was seen in 80% of cases in a study conducted by Khandelwal et al.[16]
On routine MR sequences, a normal flow void was observed in two cases and no parenchymal changes were observed, but there was evidence of thrombus on CT venography and MR venography. This finding stresses the importance of performing MR venography even though routine MR findings are normal in all suspected cases of CVT.

In the current study, 48 patients (96%) had a loss of flow void observed on conventional T1 and T2 weighted images out of 50 patients who had cerebral venous thrombosis confirmed on MRV. In 2 patients (4%) MRV confirmed CVT even though no unequivocal loss of flow void was detected on conventional MRI.

Regarding the extent of thrombosis in individual sinuses in the 50 cases, of the 120 thrombosedsinuses detected on MRV, loss of flow void was noted in only 95 sinuses (79.2%).
It's well established that false positives are common on SE sequences due to slow flow, in-plane flow and entry slice phenomenon. This coupled with the discrepancies in our study between conventional sequences and MRV in the detection of the thrombosed venous system, however non- significant statistically, reiterates the importance of MRV in combination with conventional MRI in the detection of CVT.

Leach et al[17] observed that susceptibility effects from CVT can be detected with GRE imaging and are most prevalent in patients with hypointense thrombus on T2WI within 7 days after the symptom onset. Sixty-nine thrombosed venous segments were evaluated, and thirty-six venous segments exhibited visible SE. Susceptibility artifacts from the skull base may be significant.
Isolated CVT (ICoVT) (i.e. without sinus involvement) tends to be extremely rare and has only been reported in small series or as isolated case reports. By using only T1-weighted, T2- weighted, and MRV images, ICoVT is especially difficult to be diagnosed for various reasons: cortical veins are extremely variable in number, size, and location, and small veins occluded at the cortical level are also

difficult to identify by using these MR images.

A study by M. Boukobza[18] et al shows the great value of T2*GE for the early diagnosis of ICoVT. In contrast to the transient signal-intensity changes on standard MR imaging, the cortical venous MSE observed on T2*GE images can persist for several months and possibly years after the diagnosis and treatment of ICoVT.

In the present study, 15 patients (28%) were found to have thrombosis of the cortical veins. 3 cases of isolated cortical venous thrombosis were detected. Among the 15 patients, all the cases were detected on T2* images due to blooming artefact whereas T1/T2 weighted images detected cortical vein thrombosis in only 7 (46.6%) of the 15 patients. However, the difference between T2* and T1/T2 weighted sequences in the detection of superficial cortical veins was statistically non- significant.

Also in the present study, 6 of the patients had thrombosis of the deep venous system. Of the 15 deep venous segments involved in these patients, MRV and T2* images detected thrombosis in all 15 segments. However, T1/ T2 images detected thrombosis in the veins of Galen in two of the patients. The difference between T2*/MRV and T1/T2 weighted sequences in the detection of thrombosed deep venous segments was statistically significant.
In 2 patients, T2* sequences also identified a thrombosed cerebellar vein, each of which was not found in any other sequence.

The above findings show the significance of T2* sequences in CVT detection. However, because of the significant susceptibility artifacts from the adjacent calvaria, T2* images were not used to detect thrombosis in the dural venous sinuses.

CONCLUSION

To summarize, the technique of choice for diagnostic assessment and follow-up of dural sinus thrombosis is MR angiography. The most comprehensive, non-invasive, safe, in-vivo diagnostic modality for vascular anatomy delineation, cerebral venous thrombosis diagnosis and its extent of involvement, parenchymal involvement, collateral circulation, prognosis prediction and follow-up is magnetic resonance venography combined with magnetic resonance imaging.

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