

Original research article

COMPARISON OF DIAGNOSTIC UTILITY OF MAGNETIC RESONANCE IMAGING SEQUENCES IN DETECTION OF ACUTE AND SUBACUTE PHASES OF CEREBRAL VENOUS THROMBOSIS

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ABSTRACT

Background: Cerebral venous thrombosis (CVT) entails imperative diagnosis since it requires urgent anticoagulation and thrombolytic treatment to reduce morbidity and mortality. Conventional MRI sequences are often depended upon for early diagnosis and treatment of CVT. There is, however, variation in signal intensity depending on CVT phases which need to be comprehended for accurate diagnosis.

Objective: To compare diagnostic efficacy of MRI sequences in detection of acute-subacute CVT using phase contrast magnetic resonance venography (PC-MRV) as reference standard.

Materials and Methods: A retrospective case-control study was done including 72 patients with partial or complete CVT on PC-MRV and 34 control patients with normal MRI findings. MRI sequences including T1WI, T2WI, FLAIR, DWI and SWI were analyzed. Sensitivity and specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) for all sequences were determined separately and collectively.

Results: Out of 72 cases, acute-early subacute CVT was present in 47.2% (group 1) and late subacute CVT was present in 52.8% patients (group 2). SWI had highest sensitivity, accuracy and NPV in group 1 (87.9%, 91.4%, 77.3%; respectively) followed by T1WI (83.1%, 82.1%, 65.8%; respectively). Both DWI and SWI had highest specificity and PPV in group 1. In group 2, T1WI, T2WI, FLAIR and SWI had high sensitivity, T1WI had highest accuracy and NPV and DWI had highest specificity and PPV. When all sequences were used collectively, they had highest sensitivity, accuracy and NPV in groups 1 and 2.

Conclusion: Multiparametric MRI has high sensitivity and accuracy for acute- subacute CVT and can be advantageous for early detection of clots in clinically suspected patients.

Key-words: cerebral venous thrombosis, magnetic resonance imaging, magnetic resonance venography, susceptibility-weighted imaging.

1. INTRODUCTION

Cerebral venous thrombosis (CVT) occurs due to clot / thrombosis formation in superficial and deep intracranial venous system (dural sinuses and veins) (1) and is a relatively

infrequent occurrence (2). However, there has been increase in incidence of CVT recently due to corona virus pandemic (3). CVT entails imperative diagnosis since it requires urgent anticoagulation and thrombolytic treatment to reduce morbidity and mortality (4,5,6). It may be hard to clinically establish CVT as it presents with broad range of clinical manifestations including headache, seizures, decreased vision, weakness, altered consciousness etc. (1,2,7). Computed tomography (CT) scanning is usually done for initial brain imaging but does not always give unambiguous diagnosis (4, 8). Magnetic resonance imaging (MRI) brain is sensitive to identify presence of intraparenchymal edema, bleed and infarction (2,8). MRI sequences such as T1-weighted (T1WI), T2-weighted (T2WI) and fluid-attenuated inversion recovery (FLAIR) sequences may show loss of normal flow-related signal void in venous sinuses in CVT (1,9).

Diffusion-weighted imaging (DWI) may show hyperintensity within venous sinuses in CVT; however, there are varying reports on DWI hyperintensity (6-83% of cases) and apparent diffusion coefficient (ADC) changes in CVT (10,11). T2* gradient-echo imaging (T2*GRE) and susceptibility-weighted imaging (SWI) can demonstrate loss of signal in acute thrombi as they show susceptibility effects (1, 12,13,14).

Magnetic resonance venography (MRV) is done for imaging of flow signal within venous sinuses and cortical veins and has high diagnostic accuracy for CVT (1). It shows absence of flow / presence of thrombus in venous system in complete thrombosis (2), hazy/ irregular margins of venous sinus in case of incomplete thrombosis or partial recanalization of thrombosis and is not affected by temporal signal alteration (8). It also reveals secondary formation of venous collaterals, and dilatation and congestion of other intracranial, scalp and facial veins (8). CVT is best detected with contrast-enhanced MRV (CE-MRV) (1,6), CT venography (CTV) (9) and digital subtraction angiography (DSA) (4,8); however, they require use of contrast agent which has inherent risks of allergies, nephrogenic systemic fibrosis etc. (4) and are not recommended in pregnancy and renal dysfunction (15). DSA is also invasive and causes radiation exposure with CTV (8).

Non-contrast phase contrast MRV (PC-MRV) has been previously reported with 100% sensitivity and 71% specificity for identifying CVT (4). It can be used as a non-invasive technique for prompt diagnosis of acute/ subacute CVT (4). MRV and DSA though preferred may not be accessible at all institutes; hence conventional MRI sequences are often depended upon for early diagnosis and treatment of CVT (5). There is however variation in signal intensity on different MRI sequences depending on CVT phases which need to be comprehended for accurate diagnosis. This study aimed at comparing the diagnostic accuracy, sensitivity and specificity of different MRI sequences (T1WI, T2WI, FLAIR, DWI and SWI) independently and in combination in detection of acute and subacute CVT using PC-MRV as reference standard.

2. MATERIALS AND METHODS

A retrospective case-control study was done in radiology department of a tertiary care academic institute from January 2020 to December 2022. Informed written consent is always taken from patients/ guardians prior to MRI for using their images and clinical information for academic/ educational/ publication purposes without revealing their identity as per departmental protocol. The medical records were reviewed and all patients who were clinically and radiologically diagnosed of partial or complete CVT and had undergone MRI brain (T1WI, T2WI, FLAIR, DWI, SWI and MRV sequences) were included. The subjects were excluded if they had brain tumors, infections, trauma, demyelination, arterial stroke,

thrombosis of cortical veins without venous sinus thrombosis, chronic CVT (symptom duration more than 30 days before undergoing MRI), previously undergone CVT treatment, artifacts in MRI images (motion artifacts, partial volume averaging, susceptibility artifacts etc.) and prior intracranial surgery.

MRI was done using a 1.5 Tesla scanner (Ingenia, Philips Healthcare) using 8-channel head coil. Routine MRI brain protocol included axial T1WI, T2WI, FLAIR, DWI and SWI. MRV was done using three-dimensional (3D) PC-MRV with VENC 10 cm/s and following parameters: TR/TE 20/5.6 ms, matrix 208x192 mm, FOV 230x230 mm, voxel 1.1 x 1.2 x 2.4, interslice gap 1.2 mm, NSA 1 and flip angle 15°. Since CE-MRV was not done routinely due to cost constraint, it was not included.

PC-MRV source images were analyzed for flow signal alteration in intracranial venous sinuses and veins. Then post-processing images with maximum intensity projection (MIP) reconstruction were evaluated to look for cut-off of flow signal to identify the sites of CVT (3,4). PC-MRV findings were used as reference standard for diagnosing CVT. PC-MRV source images were used to differentiate CVT from unilateral transverse sinus hypoplasia/aplasia. A total of 72 patients were identified from database that fulfilled the inclusion criteria. A control group of 34 patients was randomly selected from database that was diagnosed with normal MRI brain and PC-MRV findings.

All subjects of both groups were randomly arranged and conventional MRI brain images were visually evaluated without knowledge of clinical data. The venous sinuses and veins studied were superior sagittal sinus (SSS), bilateral transverse sinuses (TS), bilateral sigmoid sinuses (SIS), straight sinus (STS), bilateral internal jugular veins (IJV), and deep cerebral veins (internal cerebral veins and vein of Galen). The involvement of superficial cortical veins (CV) along with venous sinuses was also noted. Normal venous sinus and veins appear as low signal on T1WI, T2WI and FLAIR images and high signal on SWI with respect to gray matter and isointense signal to cerebrospinal fluid on DWI. CVT was regarded when iso-high signal was seen on T1WI, T2WI, FLAIR and DWI and low signal with blooming artifact (swollen with T2* hypointensity) on SWI (15).

Signal intensities in all sequences for all cases were tabulated in Microsoft Excel 2007 sheet and then compared with PC-MRV findings. Brain MRI images were evaluated for presence of venous infarcts, hemorrhage and edema. Demographic characteristics, clinical symptoms and duration of symptoms (time between symptom onset till MRI imaging) were noted. All subjects were arranged into two groups based on symptom duration- 1) acute to early subacute (less than 8 days), and 2) late subacute (8 to 30 days) (3). Statistical Package for Social Sciences (SSPS) 20 of IBM (USA) was utilized for data evaluation. Mean with standard deviation (SD) was estimated for quantifiable data and analyzed using independent T-test. Frequency with percentage was estimated for remaining data and analyzed using chi-square test. Statistical significance was considered when *P* value was less than 0.05. Sensitivity and specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) were determined for all MRI sequences separately and collectively.

3. RESULTS

In this study, there were 72 cases of CVT with mean age of 32.3+/-17.03 years (range 1-78 years) and 34 controls with mean age of 38.1+/-17.8 years (range 1.5-85 years). Among CVT cases, 24 (33.3%) were males and 48 (66.7%) were females and among controls, 13 (38.2%) were males and 21 (61.8%) were females. Headache was commonest clinical symptom/signs in CVT (70.8%) followed by papilledema (41.7%), nausea/ vomiting (34.7%), seizures and

hemiparesis (31.9% each), altered sensorium (30.5%), speech disturbance (15.3%) and visual difficulty (12.5%) and mean symptom duration was 9.2 \pm 5.8 days. Among CVT cases, venous infarct was seen in 45.8%, hemorrhage in 50% and edema in 44.4%.

Out of 72 cases, acute-early subacute CVT was present in 34 (47.2%) (group 1) and late subacute CVT was present in 38 (52.8%) patients (group 2). Group 1 had mean age of 30.7 \pm 20.1 years and group 2 had mean age of 33.8 \pm 13.8 years ($P=0.44$). In group 1, 11 (32.4%) were males and 23 (67.6%) were females and in group 2, 13 (34.2%) were males and 25 (65.8%) were females. There was no significant difference in age and gender distribution between CVT groups and controls. Mean symptom duration was 4.5 \pm 1.7 days in group 1 and 13.4 \pm 4.9 days in group 2.

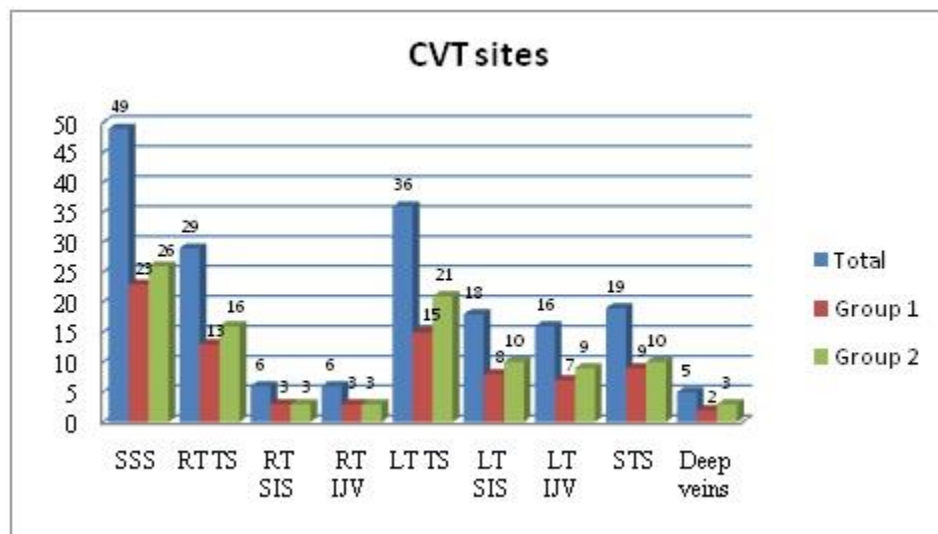


Figure 1: Sites of thrombosis in groups 1 and 2 of CVT

There were 184 sites of thrombosis among 72 CVT cases on MRV. SSS was commonest venous sinus involved (68.1%) followed by left TS (50%), right TS (40.3%) and STS (26.4%). One thrombosis site was present in 25% and more than one site in 75% cases (2-5 sites), most commonly 2 venous sites (30.6%). On MRV, 83 sites of thrombosis were noted in group 1 and 101 sites in group 2 (Figure 1). There was no significant difference in involved venous sinuses between groups 1 and 2. Additionally, cortical vein thrombosis was seen along with venous sinus thrombosis in 24 cases (33.3%), 7 cases in group 1 and 17 cases in group 2.

Out of 83 CVT sites in group 1 (Figure 2), T1WI showed iso-high signal in 69, T2WI in 55, FLAIR in 58, DWI in 39 and SWI in 73 cases. Out of 101 CVT sites in group 2 (Figure 3), T1WI showed iso-high signal in 95, T2WI in 94, FLAIR in 95, DWI in 70 and SWI in 94 cases. SWI had highest sensitivity, accuracy and NPV in group 1 followed by T1WI. Both DWI and SWI had highest specificity and PPV in group 1. In group 2, T1WI, T2WI, FLAIR and SWI had high sensitivity for CVT, T1WI had highest accuracy and NPV and DWI had highest specificity and PPV. When all sequences were used collectively, they had highest sensitivity, accuracy and NPV in groups 1 and 2 (Table 1). On evaluation of cortical veins, SWI had highest sensitivity, PPV and NPV (100% each in group 1 and 88.2%, 94.4%, 96.1%, respectively in group 2) and SWI and DWI had highest specificity and accuracy (100% each in groups 1 and 2).

Table 1: Sensitivity, specificity, accuracy, PPV and NPV of MRI sequences in CVT.

MRI sequences	Sensitivity	Specificity	Accuracy	PPV	NPV
Group 1					
T1WI	83.1%	79.4%	82.1%	90.7%	65.8%
T2WI	66.3%	70.6%	67.5%	84.6%	46.1%
FLAIR	69.9%	55.9%	65.8%	79.4%	43.2%
DWI	46.9%	100%	62.4%	100%	43.6%
SWI	87.9%	100%	91.4%	100%	77.3%
All sequences	93.9%	100%	95.7%	100%	87.2%
Group 2					
T1WI	94.1%	79.4%	90.4%	93.1%	81.8%
T2WI	93.1%	70.6%	87.4%	90.4%	77.4%
FLAIR	94.1%	55.9%	84.4%	86.4%	76%
DWI	69.3%	100%	77.03%	100%	52.3%
SWI	93.1%	70.6%	87.4%	90.4%	77.4%
All sequences	98.02%	100%	98.5%	100%	94.4%

CVT= cerebral venous thrombosis, PPV= positive predictive value, NPV= negative predictive value, T1WI= T1-weighted imaging, T2WI= T2-weighted imaging, FLAIR= fluid-attenuated inversion recovery, DWI= diffusion-weighted imaging, SWI= susceptibility weighted imaging.

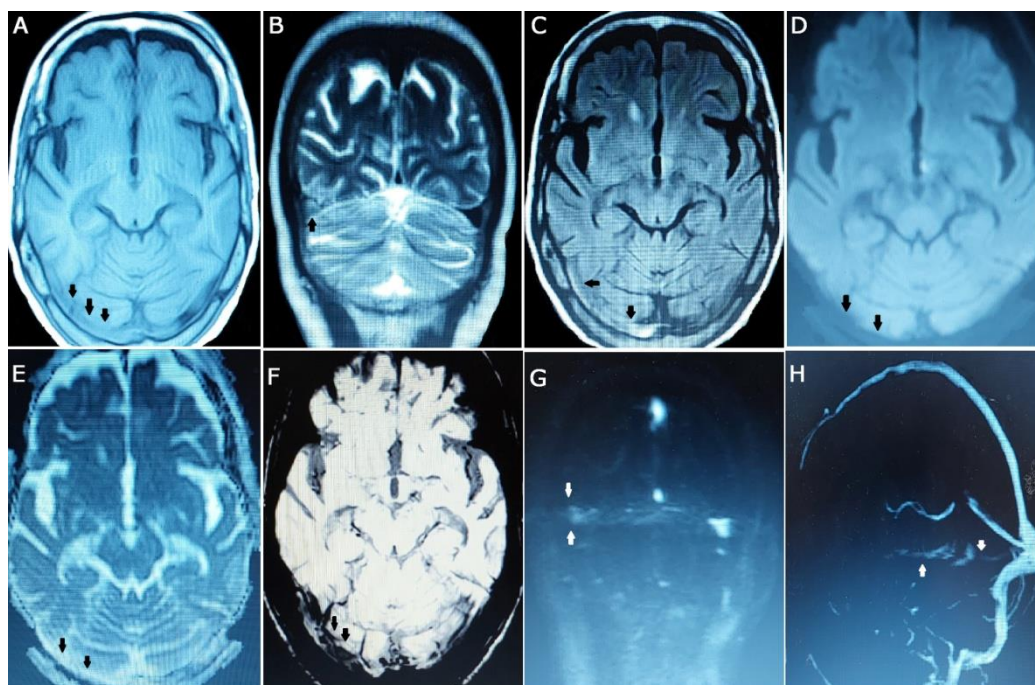


Figure 2: Partial CVT in early subacute phase in right transverse sinus showing iso signal on T1WI (A), high signal on T2WI (B) and FLAIR (C), not detected on DWI (D) and ADC (E), T2* blooming artifact on SWI (F), minimal visualization of signal on source image (G) and MIP image (H) on PC-MRV (arrows).

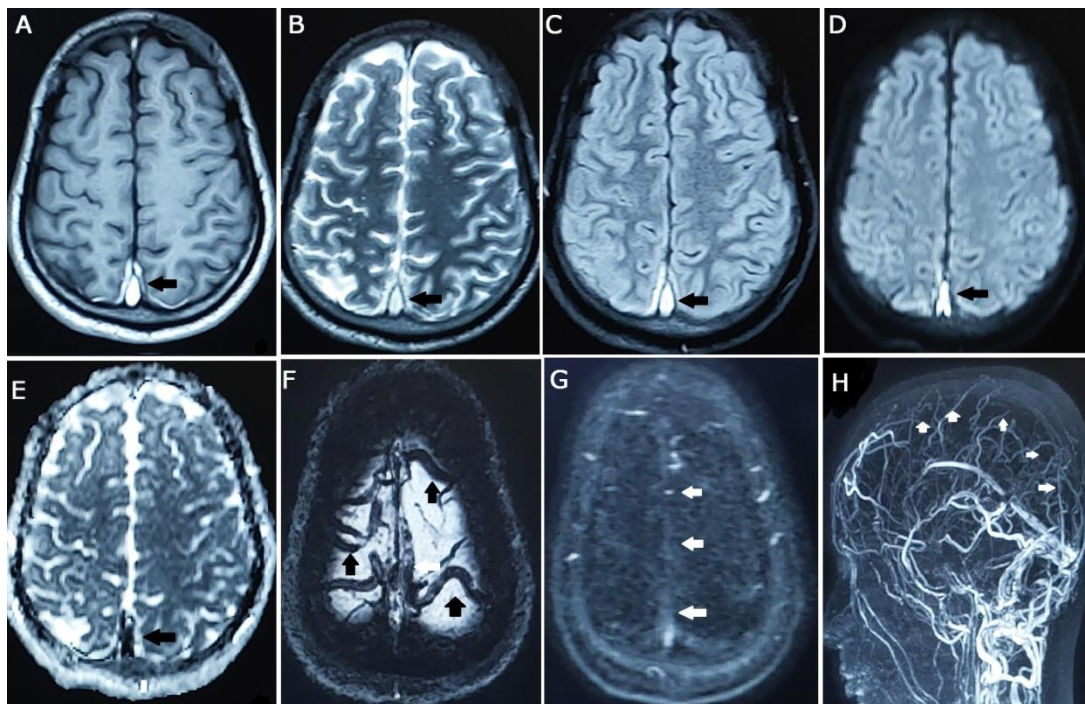


Figure 3: Late subacute complete CVT of superior sagittal sinus and cortical veins showing high signal on T1WI (A), T2WI (B), FLAIR (C), DWI (D), low signal on ADC (E), blooming artifact on SWI (F), non-visualization of flow on source image (G) and MIP image (H) on PC-MRV (arrows).

4. DISCUSSION

Thrombus formation in intracranial venous system occurs due to formation of fibrinous network along with encased red blood cells (11). CVT can cause stroke symptoms due to disruption of normal blood-brain barrier causing presence of both vasogenic and cytotoxic edema and may cause intracranial bleed (16). CVT is commoner in adult age, more frequently affecting females with subacute presentation of a wide range of non-specific and neurological symptoms and increased predisposition in diabetes, oral contraceptive intake, pregnancy, cancer, hereditary thrombophilic disorders, dehydration, autoimmune disorders etc. (4,7,17). Clinical presentation with higher proportion of females and mean age was comparable to previous studies (2,3,4). SSS, TS and SIS are most commonly affected with less frequent involvement of deep cerebral veins (6), similar to this study.

The evolution of venous clot over time causes signal changes on MRI (6,10). In acute CVT, the clot is made of deoxyhemoglobin, may appear low on T2WI and iso on T1WI (1,2,3,8). In early subacute CVT, intracellular methemoglobin shows high signal on T1WI and low signal on T2WI. In late subacute CVT, thrombus shows high signal on T2WI and T1WI (8,16) and shows decrease in signal in chronic CVT. Again, CVT may not be distinguishable from flow artifacts appearing hyperintense on T1WI and T2WI. Thrombus in early subacute CVT may appear bright on DWI with low ADC values ($< 0.55 \times 10^{-3} \text{mm}^2/\text{s}$) owing to significant restraint on passage of water molecules. Venous clots appearing bright on DWI in first scan are less likely to be recanalized on repeat scan after 2-3 months which may be related to integration of collagen and fibroblasts or atypical polymerization of fibrin (10). SWI helps in identifying blood products (deoxyhemoglobin, methemoglobin, hemosiderin, ferritin) due to local magnetic effects and show broadened, engorged veins/ sinus with prominent low signal (blooming) in CVT (7,18,19,20).

In group 1 with acute-early subacute CVT, T1WI showed iso-high signal in 83.1%, analogous to previous study (2); however, they showed lower sensitivity for T2WI and FLAIR sequences. The clot shows increase in signal in T1WI, T2WI, FLAIR and DWI with time over the first week (2) and thus their sensitivity and accuracy increased in subacute CVT. DWI was found to have lowest sensitivity in both groups, akin to previous studies (10, 11). DWI and SWI showed high specificity for CVT in comparison to other sequences, analogous to previous studies (11, 15), since high signal on DWI and blooming effects on SWI were not seen in normal venous sinuses and is particularly helpful for cases with absent flow signal on MRV. T2WI can show high signal in normal sinuses due to focal stenosis caused by arachnoid granulations, sinus hypoplasia or intra-sinus brain herniation leading to low specificity for CVT (11). In chronic CVT after four months, high signal is absent on T1WI and DWI but may be present in some cases in T2WI and FLAIR (2).

SWI showed low signal intensity (blooming effect) in most cases of acute and subacute CVT with highest sensitivity in group 1, akin to previous study by Bidar *et al.* which used T2*GRE sequence (1). Similarly, high sensitivity was reported for SWI in CVT (90%), particularly in acute phase when other sequences are less helpful (2). Blooming artifacts within clots on SWI however reduces gradually over time with reduced susceptibility effect due to extracellular methemoglobin (2,3). SWI/ T2*GRE have been shown to have maximum sensitivity for cortical vein clots, similar to this study (2). CVT can cause venous infarcts without bleed appearing heterogeneously bright on DWI having normal to high ADC values. These areas with high ADC values are indicative of viable tissues with impaired blood-brain barrier. Areas with bleed show hypointense border with peripheral low signal on DWI, central low ADC value with peripheral increased ADC value implying intracellular methemoglobin surrounded by hemosiderin rim and vasogenic edema (16). Venous infarcts can also have low ADC values similar to arterial infarcts resembling tissues at risk; however, these do not necessarily denote neuronal loss and may be reversible.

It was seen that collective use of these MRI sequences increased sensitivity, accuracy and NPV in CVT for a non-invasive, early and accurate diagnosis similar to previous studies (3,5,8). Thus, utilizing a combination of MRI sequences including non-contrast PC-MRV are favored in early diagnosis of CVT in acute-subacute phase and can be used to monitor the evolution of thrombus, cerebral venous flow, response to treatment over time and may avoid need for CE-MRV and DSA, particularly helpful in resource- limited areas where these facilities are not easily available (4, 8). DSA is an invasive technique and can be reserved for small or partial CVT to decrease possibility of false negative cases (8).

Limitations: This study was done retrospectively in one institute. Repeated imaging evaluation at intervals after starting treatment could not be done. Further studies can be done prospectively using standard MRI sequences along with CE-MRV/DSA including interval imaging of patients with CVT to better understand imaging features of thrombus in different phases of CVT.

5. CONCLUSION

Early diagnosis of CVT is favorable for better treatment response and clinical outcome. Non-invasive and non-contrast imaging using multiparametric MRI and PC-MRV have high sensitivity and accuracy for acute- subacute CVT and can be advantageous for early detection of clots in clinically suspected patients.

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Conflicts of interest: None

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