Original Article

Influence of CT/MRI Findings on Outcome and Prognosis of Patients with Cerebral Venous Sinus Thrombosis

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Objective: To study influence of CT/MR imaging findings in cerebral venous sinus thrombosis (CVST), regarding patient treatment outcome and prognosis.

Materials and Methods: The authors collected forty-two patients (n = 42) whose diagnosis of cerebral venous sinus thrombosis between 2005-2011, underwent cranial CT with contrast medium administration/CTV in all patients and contrast-MRV in 12 patients from database of Siriraj Hospital. The radiographic findings were retrospectively included in the study by one experienced radiologist. Baseline data collected included dermographic, clinical sign and presentation, vascular risk factors, treatment and outcome.

Results: From the 42 patients; 32 female (76.2%), 10 male (23,8%); mean age was 39.8 years (range 14-85 years) were identified. Symptoms included headache, vomiting, seizure, neurological deficit and blurred vision, risk factors, Glasgow coma scale (GCS), blood pressure on arrival, papilledema, hemiparesis, location of occluded venous sinuses, hemorrhagic infarction, treatment options and length of stay were analyzed to determine the outcome by using modified Rankin Scale (mRS). Poor prognosis (defined as mRS of 3-6) was determined on the discharge date. Diagnosis of venous sinus thrombosis was considered on cranial CT with contrast medium administration in 30 patients and contrast MRV in 12 patients. Radiographic findings were abnormal in all patients by thrombus location in superficial vein location: Superior sagittal sinus [SSS] (62%), Transverse sinus [TS] (64%), sigmoid sinus (69%), internal jugular vein (50%), cortical vein (31%) and deep vein location: internal cerebral vein (5%). Those with deep vein involvement (5%) and parenchymal involvement (55%) had poor outcome 100% and 88.9% after heparin treatment, respectively.

Conclusion: Although, overall prognosis was good outcome in 78% of patients, patients with parenchymal involvement (Hemorrhage, infarction, midline structure shifting, brain swelling, brain herniation, hydrocephalus) were more likely to present in poor outcome.

Keywords: CT/MRI, Cerebral venous sinus thrombosis

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The diagnosis of cerebral venous sinus thrombosis may be very difficult due to the large spectrum of clinical manifestations and the multiple associated conditions and etiologies[1,3,8]. Cerebral venous sinus thrombosis [CVST] was considered to be a rare disease with high morbidity, but more recent studies indicate that this condition is more frequent and more benign than previously thought[1,8-11]. Risk factors for CVST included inherited thrombophilia, acquired prothrombotic state, systemic disease (e.g. SLE), neoplasia (leukemia, systemic carcinoma), systemic infectious disease (e.g. septicemia), local causes (e.g. otitis, mastoiditis) and use of oral contraceptives[3,10,12].

Multidetector CT [MDCT] or Magnetic resonance imaging [MRI] is nowadays accepted as the first line study of suspicious of CVST[3]. The routine protocol MDCT of brain includes non-contrast phase (NECT) and CT with contrast phase either post-contrast phase or CTV phase. The NECT is better to evaluate intracerebral hemorrhage, so preferable to screening for emergency condition in patients with neurological symptom. And the MRI scan is also superior to conventional CT for diagnosis CVST[3]. CVST is an emergency condition requiring accurate diagnosis and prompt treatment to reduce its potentially serious consequence and mortality. In an acute phase, identification of poor prognostic factors is essential in order to select the best therapeutic strategy and management of modifiable factors to improve treatment outcome and prognosis.

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Our aim of the present study was to determine 42 patients with CVST influenced on clinical outcome and prognosis by using modified Rankin scale [mRS]. In addition, this study was to determine whether the neuroimaging features influenced outcome and prognosis in these patients.

Materials and Methods

Subjects

From January 2005 to December 2011, the authors collected the patients diagnosed as cerebral venous sinus thrombosis whom underwent CT brain with contrast medium administration or MRI/ MRV brain study. CT brain with contrast medium administration was performed in all patients and MRV in twelve patients. The diagnosis of CVST had been documented by neurologists with the evidence of thrombosis in cerebral venous sinus on computerized tomography (CT scan) of the brain with contrast medium administration and contrast-enhanced MRV brain. The exclusion criteria were patients who did not have neuroimaging on PACs system and the patient whose medical record could not be collected.

Finally, the forty-two patients [(n = 42, female = 32 (76.2%), male = 10 (23.8%)] who diagnosis of CVST that supported by appropriate neuroimaging studies including "empty delta sign" on cranial computed tomography [CT] with contrast medium administration, a partial or complete absence of filling of one dural sinus on two projections using contrast-enhanced Magnetic resonance venography [MRV] was used as additional evidence whenever possible.

The patients were recorded in data of gender, age, presenting symptoms and signs, risk factor, neuroimaging : location of thrombus, parenchymal involvement, associated findings : infarction, hemorrhage, shifting of midline structure, brain swelling, brain herniation, hydrocephalus, treatment and outcome by using modified Rankin Scale (mRS). Poor prognosis (defined as mRS of 3-6), and good outcome (defined as mRS of 0-2) were determined on the discharge date.

Imaging Investigation

The site and extent of the thrombus and the appearance of associated brain lesions were determined for all patients.

MDCT Protocol

All CT examinations were done with 64-slice multidetector-row computed tomography (MDCT) (Siemens and General Electric medical systems). Following parameters: 120 KV tube voltage, field of view: head, 300 mA tube current, detector combination 64 x 1.25 mm and 64 x 1.5 mm, axial mode. The whole brain scan was covered from the skull base to the vertex.

MRI Protocol

MRIs were performed in a 1.5T scanners (Siemens, Erlangen, Germany) by following sequences: DWI-sequence, T2-weighted SE-sequence, T1-weighted SE-sequence, T2*-weighted gradient-echo sequence, FLAIR sequence, including T1WI/GD MRV images.

Image Analysis

Review of all imaging examination was conducted with one neuroradiologist.

Evidence of cerebral venous sinus thrombosis was "empty delta sign" on cranial computed tomography [CT] with contrast medium administration, a partial or complete absence of filling of one dural sinus on two projections using contrast-enhanced MRV.

Location of involving venous sinuses were divided as:

- Dural venous system: superior sagittal sinus [SSS], inferior sagittal sinus [ISS], transverse sinus [TS], Straight sinus, Sigmoid sinus [SS], internal jugular vein [IJV],
- Superficial cortical vein
- Deep venous system: internal cerebral vein [ICV], vein of Galen, basal vein of Rosenthal and thalamostriate vein.

Associated findings:

- Parenchymal involvement was defined as evidence of lesion in brain parenchyma which relation to drainage of venous sinus thrombosis. Either cerebral infarction or intracerebral hemorrhage was defined as hypoattenuating area on CT, hypersignal intensity on T2W with restrictive diffusion on DWI image or hyperattenuating area on CT or hypersignal intensity on T1W image, respectively.
- Brain swelling was defined as localized of generalized in loss of gray-white matter differentiation, increase water contents which appeared hypoattenuation on CT scan and increase signal intensity on T2W image.
- Brain herniation was defined as the displacement of brain from one cranial compartment to another.
- Hydrocephalus was defined as abnormal accumulation of cerebrospinal fluid [CSF] in the ventricular system dilatation.

The relevant parameters of treatment during hospitalization were recorded including anticoagulant treatment (unfractionated heparin, low molecular weight heparin, warfarin), other medical supportive treatment such as antiepileptic agents, surgical treatment and duration of admission. The outcome at discharge was assessed with the modified Rankin Scale (mRS)[1,3], with the patients with mRS scores 0 to 2 being classified as independent survivors (good outcome), and patients with mRS scores 3 to 6 being classified as dependent or dead (poor outcome), shown in Table 1.

Modified Rankin scale, mRS 0-6

0 = no symptoms

1 = no significant disability, despite symptoms, able to perform all usual duties and activities

2 = Slight disability, unable to perform all previous activities but able to look after own affairs without assistance

3 = Moderate disability, requires some help, but able to walk without assistance

4 = Moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance

5 = Severe disability, bedridden, incontinent, and requires constant nursing care and attention

6 = Dead

Statistical Analysis

Univariable analysis was performed to categorize patients with good and poor outcomes. Unpaired t-test was used for quantitative data that was normally distributed (e.g. age, GCS, blood pressure). For quantitative variables, Pearson's Chi-square test was employed.

Multivariable analysis using each parameter was performed to determine the effect of each predictor on developing poor outcome. Adjusted odds ratio [OR] with a 95% confidence interval [CI] and parameter estimates influence of poor outcome were applied. All statistical analyses were performed using SPSS version 13.0.

Results

Characteristics of patient population included baseline characteristics, clinical, neuroimaging parameters between two groups are shown in Table 1. From the 42 patients, 32 patients were female and the other 10 were male. The mean age was about 39.8 years (range 14-85 years).

The patients presented with multiple presentations. Most common presentation was headache (71%), followed by vomiting (31%), Seizure (31%), neurological deficit (38%), blurred vision (29%). Most common identifiable risk factors were contraceptive pill usage [16/42 938%)], followed by CNS disease [5/9 (12%)]. Nine of 42 (21.4%) patients were in the poor outcome group, and 33 of 42 (78.6%) patients were in the good outcome group.

Neuroimaging studies were available for review in all patients. Cranial CT with contrast medium administration was performed in all patients and MRV in 12 patients.

Diagnosis of venous sinus thrombosis was considered on cranial CT with contrast medium administration in 30 patients and MRV in 12 patients. The radiographic findings were abnormal in all patients by location of thrombus, the majority of the involved venous sinuses were sigmoid sinus [29/42 (69%)], followed by transverse sinus [27/42 (64%)], superior sagittal sinus [26/42 (61.9%)], internal jugular vein [21/42 (50%)], cortical vein [13/42 (31%)] and internal cerebral vein [2/42 (5%)]. One patient had involvement of a dural sinus in addition to deep cerebral vein involvement. All of 2 patients with deep cerebral vein involvement had poor outcome or death (mRS = 6). Degree of involvement and location of sinus involvement in good and poor outcome groups of patients is shown in Table 2.

Nine patients (21.4%) were in poor outcome group (mRS 3-6) and Thirty-three patients (78.6%) were in good outcome group (mRS 0-2). All of those, eight patients [8/9 (88.9%)] had parenchymal involvement. Thirteen patients (30.9%) had intracerebral hemorrhage and nearly half [6/13 (46%)] of those were in the poor outcome group. Three patients (7%) had brain herniation and more than half [2/3 (66.7%)] of those were in the poor outcome group.

All patients were treated with dose-adjusted IV heparin or low molecular weight heparin (LMWH). Thirty-three patients (78.6%) were stabilized and later improved were in good outcome. Heparin was then switches to oral anticoagulants. Nine patients (21.4%) were deteriorated rapidly, with four patients progressing coma and then death (mRS = 6), five patients were of stabilized group (mRS 3-5). All of 9 patients received heparin treatment alone.

Table 3. demonstrates odds ratio (OR) and 95% CI of OR of additional CT findings in patients with venous sinus thrombosis and poor outcome after treatment

Table 1. Comparison of baseline patients' characteristics, risk factors, physical examinations and neuroimaging findings between poor and good outcomes

Characteristics	Poor outcome (n = 9)	Good outcome (n = 33)
Dermographic data		
- Age (year) (x̄±S.D.)	48.56±20.8	37.45±13.2
- Male : female	2 : 7	8 : 25
Clinical presentation (n (%))		
- Headache	2 (22.2)	28 (84.8)
- Vomiting	2 (22.2)	11 (33.3)
- Seizure	5 (55.6)	8 (24.2)
- Neurological deficit	5 (55.6)	11 (33.3)
- Blurred vision	2 (22.2)	10 (30.3)
Characteristics	Poor outcome (n= 9)	Good outcome (n=33)
Risk factors (n (%))		
- Infection	1 (11.11)	3 (9.1)
- Contraceptive agent	1 (11.11)	15 (48.5)
- CNS disease	2 (22.2)	3 (9.1)
- Malignancy (n (%))	2 (22.2)	2 (6.1)
- Hematologic disorder	-	3 (9.1)
- No U/D	3 (33.3)	6 (18.18)
Physical examination (x̄±S.D.)		
- GCS	12.22 ± 3.1	14.27 ± 2.4
- SBP	128.0 ± 22.1	125.9 ± 20.9
- DBP	76.56 ± 11.4	77.88 ± 13.1
- Papilledema (n (%))	1 (11.1)	20 (60.6)
- Hemiparesis (n (%))	9 (100)	12 (36.4)
- Meningeal sign (n (%))	4 (11.1)	2 (6.)
Location of VST		
Dural venous system (n (%))		
- SSS	5 (55.6)	21/33 (63.6)
-TS	3 (33.3)	24/33 (72.7)
- Straight sinus	6 (66.7)	23/33 (69.7)
- Sigmoid sinus	2 (22.2)	19/33 (57.6)
- IJV	2 (22.2)	11/33 (33.3)
Superficial cortical vein		
Deep vein (n (%))		
- Vein of Galen	-	-
- Internal cerebral vein	2 (22.2)	-
- Basal vein of Rosenthal	-	-
- Thalamostriate vein	-	-
Parenchymal involvement	8 (88.9)	15 (45.46)
- Unilateral	5 (55.6)	5 (15.16)
- Bilateral	3 (33.3)	10 (30.30)
No parenchymal involvement	1/9 (11.1%)	18 (54.54)
Associated findings : (n (%))		
Infarction	4 (44.4)	7 (21.2)
Hemorrhage	6 (66.7)	7 (21.2)
- Intracerebral hemorrhage	4 (44.4)	6 (18.2)
- Subarachnoid hemorrhage	1 (11.1)	1 (3.0)
- Intraventricular hemorrhage	1 (11.1)	-
Shifting of midline	1 (11.1)	2/33 (6.1)
Brain swelling	8 (88.9)	16/33 (48.5)
Brain herniation	2 (22.2)	1/33 (3.0)
Hydrocephalus	2 (22.2)	2/33 (6.1)
Treatment : (n (%))		
Anticoagulant	9 (100)	28 (84.8)
Surgical intervention	-	-
Observation	-	4/33 (12.1%)
Antiepileptic drugs	-	1/33 (3%)
Duration of admit (days) (x̄±S.D.)	35.44±46.4	13.12±8.4

Table 2. Characteristics by location of dural sinus involvement (n=16) : superior sagittal sinus and transverse sinus with or without dominant sinus

Characteristics (n (%))	Poor outcome (n = 3)	Good outcome (n = 13)
Partial SSS + TS (Dominant)	-	7 (53.84)
Partial SSS + TS (Non-dominant)	-	3 (23.08)
Extensive SSS + TS (Dominant)	1 (33.33)	3 (23.08)
Extensive SSS + TS (Non-dominant)	2 (66.67)	-

Table .3 Results of poor outcome

Factors	Odds ratio (OR)	95% CI
Infarction	2.97	0.626 to 14.102
Hemorrhage	7.43	1.47 to 37.45
Shifting of midline structure	1.94	0.155-24.156
Brain swelling	8.50	0.953-75.804
Brain herniation	9.14	0.724-114.459
Hydrocephalus	4.43	0.529-37.067

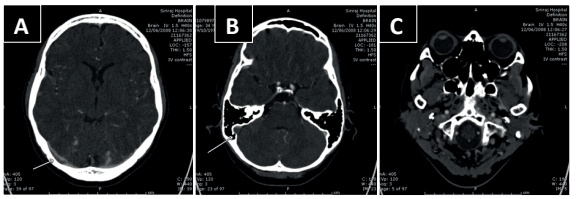

Figure 1. A 34 year-old female presented with symptoms of severe headache, blurred vision with nausea and vomiting for 4 days. She had been taking oral contraceptive pills for 26 years. The physical examination on admission revealed good consciousness with GCS of 15. The physical examination on admission revealed papilledema. An emergency CT of the brain was performed with the result showing long segment of occlusion of right transverse-sigmoid sinus (A-B) down to right internal jugular vein (C). The diagnosis of CVST right transverse sinus, right sigmoid sinus and right internal jugular vein was confirmed. Pretreatment mRS score = 2, then after anticoagulant therapy was given, posttreatment mRS score = 1 good outcome.

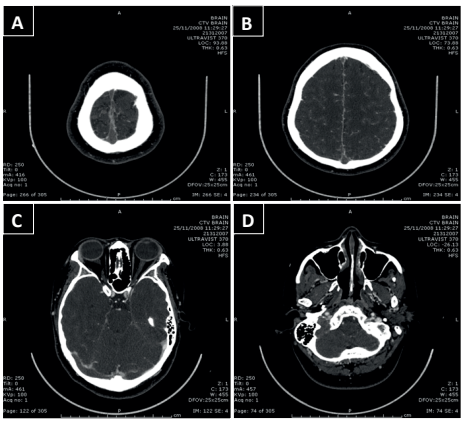

Figure 2. A 27 year-old female presented with symptoms of severe headache, nausea and vomiting for 3 days. She had been taking oral contraceptive pills for 3 months. Physical examination on admission revealed good consciousness with GCS of 15. The physical examination on admission revealed papilledema. An emergency CT brain was performed with the result showing long segment of occlusion of SSS (A-B), right transverse sinus (C) down to right internal jugular vein (D). The diagnosis of CVST SSS, right transverse sinus, right sigmoid sinus and right internal jugular vein was confirmed. Pretreatment mRS score = 3, then after anticoagulant therapy, posttreatment mRS score = 1 good outcome.

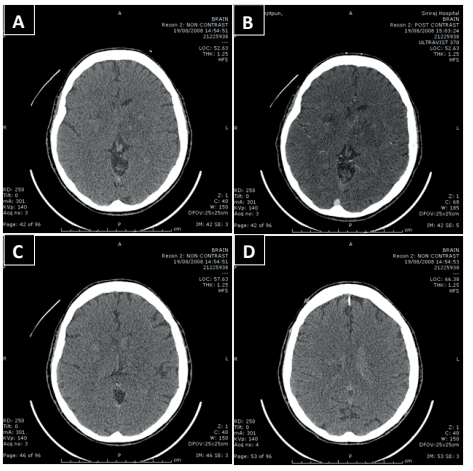

Figure 3. A 48 year-old woman with known diagnosis of NF1, presented with a recent onset of global aphasia, GCS 11/15. CT brain non-contrast study revealed clot in bilateral internal cerebral veins, intracerebral hemorrhage at bilateral thalamus with edema (A,C) and intraventricular hemorrhage in frontal horn of both lateral ventricles, no brain herniation (D). CT brain with contrast study showed filling defect in bilateral internal cerebral veins that confirmed deep cerebral venous sinus thrombosis (DCVST). Pretreatment mRS score = 5, then after anticoagulant therapy with no surgical intervention and she died ten days later with no autopsy, posttreatment mRS score = 6 poor outcome.

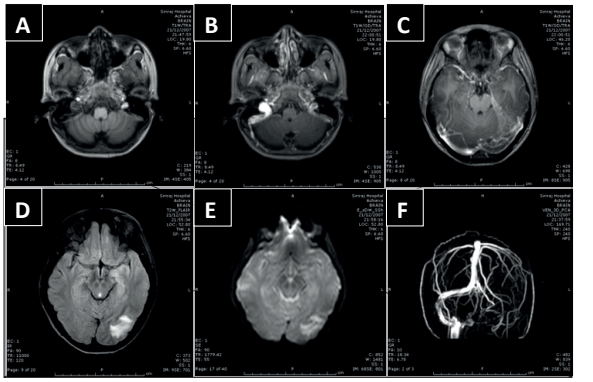

Figure 4. A 19 year-old woman presented with symptoms of severe headache and blurred vision for 5 days. She had been taking oral contraceptive pills for 6 months. Physical examination on admission revealed good consciousness with GCS of 15. CTV brain was performed suspicious of cerebral venous thrombosis, then contrast MRV was done with the result showing long segment of occlusion of left transverse sinus down to left sigmoid sinus and left internal jugular vein on axial T1-weighted image (A), axial T1-weighted image with Gadolinium administration (B,C) and contrast-MRV (F). Axial T2/FLAIR (D) showed increase signal intensity with restrictive diffusion (E) at left temporal region, represented venous infarction. The diagnosis of CVST at left transverse sinus, left sigmoid sinus and left internal jugular vein was confirmed. Pretreatment mRS score = 5, then after anticoagulant therapy, posttreatment mRS score = 0 good outcome.

Discussion

The mean age of the presented patients was 39.8 years with female predominately, which was close to previous studies[1-5]. In addition, the present study also revealed the similar results on location, percentages of the involved venous sinuses and imaging on hemorrhagic infarction in comparison to the International Study on Cerebral Vein and Dural Sinus Thrombosis [ISCVT], the largest multicenter international study[9]. Disturbance of cerebral venous drainage due to CVST may lead to irreversible or permanent brain lesions[3,10,11]. The clinical onset is variable and nonspecific, including headache, motor or sensory deficits and seizures. The neurological symptoms and signs encountered in our series were those classically associated with CVST[1-3,10,11]. Headache was the most frequent symptom, referred by 71% of patients, in correlation with previous reported[3,10,11].

The recent improvement in MRI techniques and multi-slice contrast-enhanced CT had improved diagnosis of CVST. Cranial CT was still the first

examination done in most cases, mostly because it is readily available in most emergency services, and its short scanning time and ability to detect acute hemorrhage[3,10]. The cord sign and the delta sign in enhanced CT refer to imaging signs suggestive of CVST[3,5-7]. CTV using a multi-slice technique has been reported to be superior to CT and an alternative to MRI and MRV, although not yet used routinely in most services.

CVST was associated with coagulation defects or risk factors such as hormonal therapy, pregnancy or increased blood viscosity in about 75% of cases[3]. In our series, etiologies were identified in 76% of the patients. Most frequent cause of this series was contraceptive usage about 38% of these patients[3,9].
In this series of forty-two patients with cerebral venous sinus thrombosis, thirty-three patients (78.57%) had a favorable outcome, excellent recovery or minor handicaps (mRS $\leq$2) which able to return to their previous job, activity or education. This suggests that recovery form neuropsychological deficits were good in most patients[3,10]. Nine patients (21.4%) had a poor outcome, four of those patients died despite maximally supportive treatment. A number of factors contributed to the poor results in these patients. In 4 patients was died, 2 patients of those with deep internal cerebral vein thrombosis, both (100%) represented poor prognosis[1-3], but they contrast with a recent report of ISCVT[10], in which 71% of patient with deep cerebral venous thrombosis lived independently at follow up. In our series, this poor outcome in deep cerebral venous sinus thrombosis might be partly explained by the additional involvement of parenchymal involvement, all presented in 2 patients (100%) of these patients with deep cerebral venous sinus thrombosis.

The present study, additional CT findings: intracerebral hemorrhage, brain herniation and brain swelling were significant more likely to poor outcome with deep cerebral vein thrombosis. Comparable to those of the previous studies[1-3,9,10], our finding was in accordance with previously reported findings, in which intraparenchymal involvement documented by CT or MRI especially intracerebral hemorrhage had increase in risk of suffering neurological sequel, brain herniation was the most common cause of death in patients with CVST and extensive SSS thrombosis could be lead to poor outcome, especially extensive SSS thrombosis and TS (non-dominant) thrombosis as shown in Table 2.

Two patients with dural venous sinus thrombosis: SSS, TS and sigmoid sinus (dominant TS-SS) included additional CT findings : ICH, brain herniation and brain swelling, both were died which one patient had hematologic malignancy with CNS involvement with posterior 1/3 SSS, cortical vein, right TS (dominant TS-SS) and another patient had DM with sepsis with extensive dural venous sinus thrombosis at SSS, bilateral TS, SS, IJV (partial). The authors found that underlying condition such as malignancy or systemic infection was the risk factor for poor outcome similar to other studies.

In adult and pediatrics CSVT, anticoagulant appeared safe[9-11]. All patients in our study received heparin (keep INR 2-3) followed by oral anticoagulants. No clinical worsening after introduction of heparin or signs of further intracranial hemorrhage on follow up scans was observed in this series. In addition to heparin treatment, local thrombolysis has been reported in small series[1,3-4,11,12]. In our series, lack of anticoagulant treatment was not inevitably associated with death or severe long term disability in our patients: 4 patients (mRS 2-5) in whom conservative treatment or antiepileptic drugs, because the clinicians considered it made risk more than benefit (previous ICH), then follow up these patients had a good outcome (mRS = 2, all). However, local thrombolysis able to lyse the thrombus more rapidly that heparin had made thrombolysis and alternative option in CVST treatment. Local thrombolysis is not considered first line treatment because of higher risk of cerebral hemorrhage and the absence of correlation between the resolution of thrombosis and clinical improvement. Until further evidence, local thrombolysis should be used when heparin treatment fails[1,3,4].

The methodological limitation of the present study was small sample size (42 patients) which some potential inclusion bias and unreliable statistically significant. Retrospective nature of data analysis was performed. As a result, some information was not available pertaining to details and timing of investigation, clinical follow-up information or follow up study.

Based on our study results, location, size and extension of parenchymal involvement including staging or the length of thrombus on MRI study in patient with cerebral venous thrombosis have been performing to evaluate the patients 'outcome and prognosis and may warrant the future study.

What is already known on this topic?

Multidetector CT (MDCT) or Magnetic resonance imaging (MRI) is nowadays accepted as the first line

study of suspicious of CVST. The routine protocol MDCT of brain includes non-contrast phase (NECT) and CT with contrast phase either post-contrast phase or CTV phase. The NECT is better to evaluate intracerebral hemorrhage, so preferable to screening for emergency condition in patients with neurological symptom. And the MRI scan is also superior to conventional CT for diagnosis CVST. CVST is an emergency condition requiring accurate diagnosis and prompt treatment to reduce its potentially serious consequence and mortality.

What this study adds?

In an acute phase, identification of poor prognostic factors is essential in order to select the best therapeutic strategy and management of modifiable factors to improve treatment outcome and prognosis. In summary, our data confirm that the diagnosis of CVST had a wide variety of clinical presentations. Patients with parenchymal involvement (intracerebral hemorrhage and brain swelling) were more likely to present neurological sequelae or poor outcome. The overall prognosis is good in 78% of patients but progressing coma with poor outcome still occurs despite heparin treatment in some patients in whom endovascular therapy may be considered as an additional therapeutic option.

Potential conflicts of interest

The authors declare no conflict of interest.

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