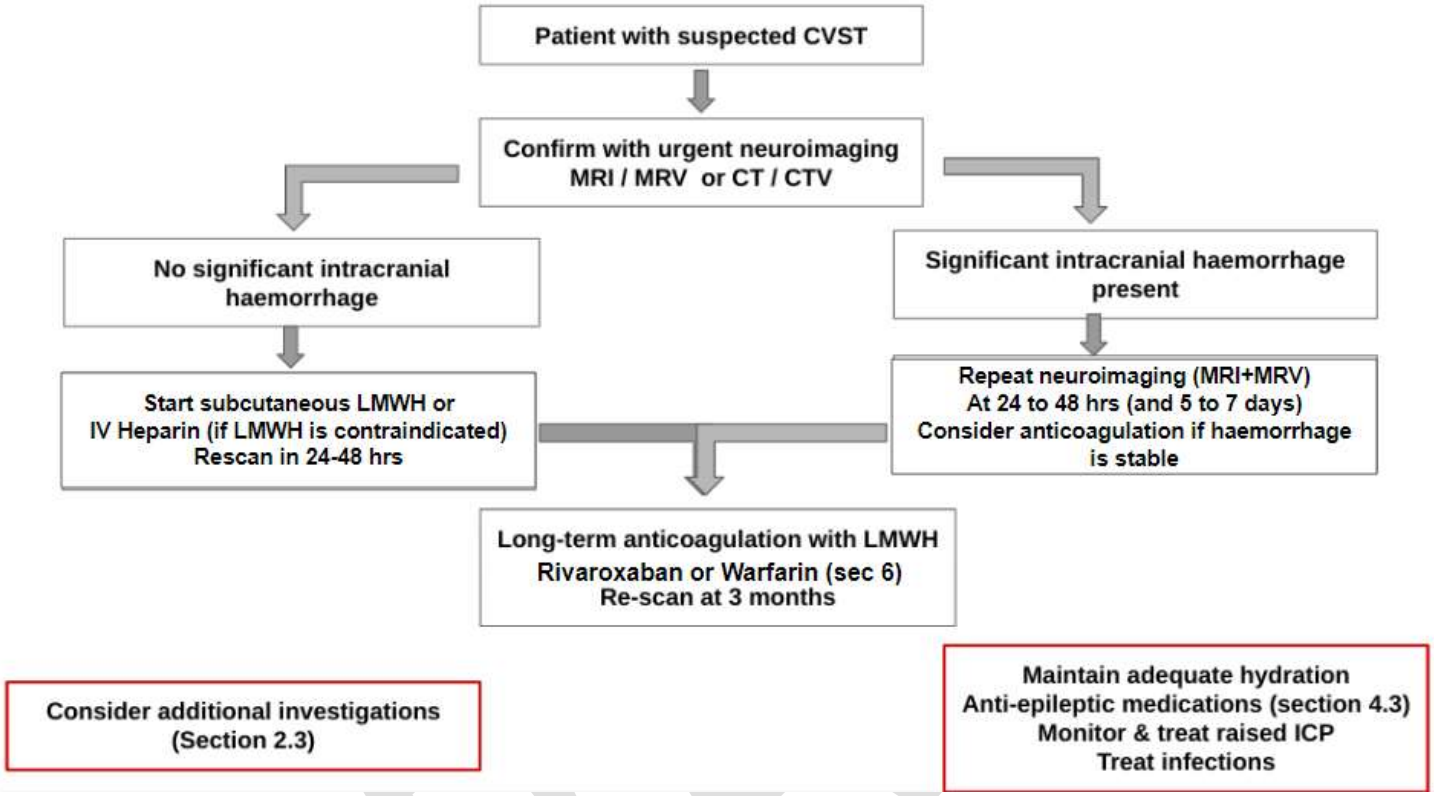
Cerebral venous sinus thrombosis (CVST) guideline



1. Pathogenesis and clinical presentation

1.1 The pathogenesis of CVST remain incompletely understood. The known mechanisms are

- Thrombosis of cerebral veins or dural sinus obstructs drainage of blood from brain parenchyma, leading to cerebral parenchymal lesions (eg, stroke- haemorrhagic infarcts) or dysfunction and increased venous and capillary pressure with disruption of the blood-brain barrier
- Occlusion of dural sinus result in decreased cerebrospinal fluid (CSF) absorption and elevated intracranial pressure.

1.2 Common risk factors in children:

- Infections (including sinusitis, mastoiditis)
- Dehydration
- Head injury and mechanical precipitants
- Prothrombotic conditions, either genetic or acquired.
- Malignancy

1.3 Common signs and symptoms:

- **Headache** is the most frequent symptom of CVST, other symptoms include:
- Symptoms of Isolated **intracranial hypertension**: headache with or without vomiting, papilledema, and visual problems
- Focal symptoms: focal neurological deficits, **seizures**, or both
- **Encephalopathy**: multifocal signs, mental status changes, stupor, or coma
- Symptoms due to isolated sinus or vein thrombosis
    - Cavernous sinus thrombosis shows predominantly ocular signs with orbital pain, chemosis, proptosis, and oculomotor palsies
    - Isolated cortical vein occlusion may present with motor/sensory deficits and seizures
    - Sagittal sinus occlusion can cause bilateral motor deficits, and seizures (presentation as an isolated intracranial hypertension syndrome is infrequent)
    - Isolated lateral sinus thrombosis: present with isolated headache, isolated intracranial hypertension, focal deficits or seizures
    - Jugular vein or lateral sinus thrombosis may present as isolated pulsating tinnitus
    - Multiple cranial nerve palsies may occur in thrombosis of the lateral sinus, jugular, or posterior fossa veins

2. Diagnostic approach

2.1 A diagnosis of CVST should be suspected in patients who present with one or more of the following:

- New-onset severe headache with no cause identified
- Symptoms or signs of intracranial hypertension
- Encephalopathy
- Focal neurological deficits, especially those not fitting a specific vascular distribution or those involving multiple vascular territories.
- Seizures (predominantly focal)

2.2 In patients with suspected CVST, urgent neuroimaging is required:

Brain MRI with MR venogram (MRV) is the preferred imaging modality. **A Cranial CT with CT venogram** could be requested if MRI is not an option.

- The absence of flow and presence of an intraluminal venous thrombus by CT or MRI is the most important finding to confirm the diagnosis.
- The characteristics of the MRI signal depend on the age of the thrombus.

    - In the first five days, the thrombosed sinuses appear isointense on T1-weighted images and hypointense on T2-weighted images.
    - Beyond five days, venous thrombi become more apparent with increased signal on both T1- and T2-weighted images.
    - After the first month, thrombosed sinuses exhibit a variable pattern of signal, and may appear isointense.

- Several normal anatomic variants may mimic sinus thrombosis, including sinus atresia, sinus hypoplasia, asymmetric sinus drainage, and normal sinus filling defects associated with arachnoid granulations or intrasinus septae.

2.3 Other specific investigations:

2.3a. D-dimer — An elevated plasma D-dimer level supports the diagnosis of CVST, but a normal D-dimer does not exclude the diagnosis in patients with suggestive symptoms and predisposing factors

2.3b Lumbar puncture - may be useful to exclude meningitis in patients with CVST who present with isolated intracranial hypertension, OR to measure and decrease cerebrospinal fluid (CSF) pressure when vision is threatened

2.3c. Evaluation for thrombophilic state — this is indicated in patients with CVST with a personal and/or family history of venous thrombosis and in cases of CVST without a transient or permanent risk factor.

Seek advice from Haematology team in such cases. The recommended **screening tests** include:

- Antithrombin, Protein C, Protein S, Factor V Leiden
- Prothrombin G20210A pathologic variant
- Lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein-I antibodies
- Homocysteine

In practice, **it is preferable to test for protein C, protein S, and antithrombin at least two weeks after oral anticoagulation has been discontinued.**

- Acute thrombosis can transiently reduce levels of antithrombin, protein C, and protein S, so the utility of these tests in the acute phase of CVST is limited.
- Warfarin therapy reduces protein C and protein S levels and may raise plasma antithrombin concentrations into the normal range in patients with hereditary antithrombin deficiency.
- Heparin therapy does not alter plasma protein C or protein S concentrations but can lower antithrombin levels. It is possible to test for protein C and protein S levels

while receiving heparin. However, testing for antithrombin should be performed when off heparin.

3. Treatment of CVST:

The goals of acute treatment of CVST are:

- To prevent the propagation of the thrombus, namely to the bridging cerebral veins
- To recanalize the occluded sinus/vein
- To treat the underlying prothrombotic state, in order to prevent venous thrombosis in other parts of the body, particularly pulmonary embolism, and to prevent the recurrence of CVST

3.1 Initial anticoagulation (seek haematology advice)

Anticoagulation with **subcutaneous Low molecular weight heparin (LMWH)** is recommended in most children with CVST except in the following situations where IV heparin is preferred

3.2 Indications for intravenous unfractionated heparin (UFH)

- patient is clinically unstable
- invasive interventions such as lumbar puncture or surgery are planned
- LMWH is contraindicated e.g. in kidney failure

Limited data from adults suggest that LMWH is more effective than UFH and at least as safe for the treatment of CVST

3.3 Anticoagulation in patients with existing haemorrhage:

For children with CVST who have significant intracerebral haemorrhage such as haemorrhagic venous infarction, the ACCP guideline (see reference) suggests either

a. Initial anticoagulation as for children without haemorrhage ***OR***
b. Radiological monitoring of the thrombosis at 24 to 48 hrs and between days five and seven and consider anticoagulation if the haemorrhage is stable ***OR*** thrombus extension is noted at that time.

Data from adult studies show that anticoagulation is safe to use in patients with CVST who have associated intracerebral or subarachnoid haemorrhage. But this needs to be carefully considered in paediatric population.

4 Other management in the acute phase

4.1 Hydration - Optimal hydration should be maintained in all patients with CVST.

4.2 Raised intracranial pressure - patients need monitoring and intervention as required for raised intracranial pressure (follow the raised ICP guideline) and discuss with neurosurgical team at an early stage.

4.3 Seizures - Antiepileptic medication is recommended for patients with CVST who have seizures or show focal cerebral lesions such as oedema or infarction on initial neuroimaging.

4.4 Infection - Patients with suspected intracranial infection or an infection of a neighbouring structure (sinusitis, otitis or mastoiditis) need antibiotic treatment.

5. Radiological monitoring: Arrange radiological monitoring (MRI/MRV) at 24-48 hours regardless of commencement of anticoagulation therapy needs to be considered to monitor thrombus propagation.

6. Children with severe CVST not improving with initial anticoagulation therapy: Patients who show progressive neurological deterioration despite adequate anticoagulation may be considered for endovascular thrombolysis, mechanical thrombectomy or surgical decompression (seek neurosurgical advice)

7. Long term anticoagulation treatment

Initial anticoagulation with UFH or LMWH should be followed by **LMWH, Rivaroxaban** (a direct inhibitor of activated factor X - factor Xa) **or Warfarin** (Vitamin K antagonist treatment) **for a minimum of three months** in children with CVST. (Please seek advice from haematology team)

If the repeat MRI/MRV after three months of therapy show persisting cerebral sinovenous occlusion or if the patient has ongoing symptoms (e.g., of raised intracranial pressure), an additional three months of anticoagulation treatment is recommended.

References:

1. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Monagle et al, American College of Chest Physicians, Chest. 2012 Feb;141(2 Suppl):e737S-801S.
2. Cerebral venous thrombosis - Uptodate
3. Anil S, Hudson G, Fung A, et al1614 Paediatric cerebral venous sinus thrombosis (CVST): a single-centre audit and discussion of best practice Archives of Disease in Childhood 2021;106:A429-A430