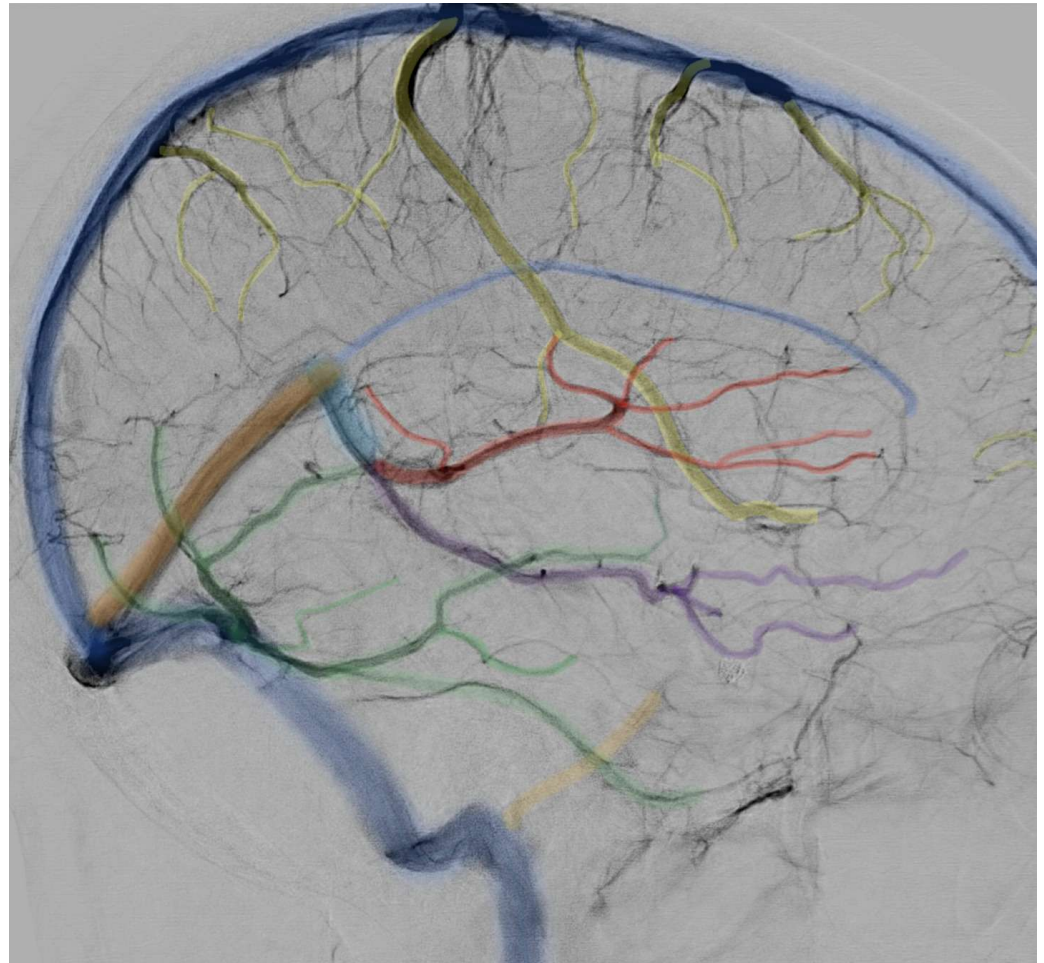


Cerebral venous thrombosis (CVT)

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Outline

Introduction and Epidemiology

Risk Factors

Anatomy and pathogenesis

Clinical features

Imaging Diagnosis

Management and Treatment

Prognosis

What is CVT?

- Definition: Thrombosis in the cerebral veins and dural sinuses.

Epidemiology:

- Rare but significant: estimated incidence of 5 people per million annually.
- 0.5-1% of all strokes, but important cause of stroke in young adults.
 - The mean age of onset is 39 years old.
 - 78% occurred in patients younger than 50.
- CVT is more common in females than males, with a female-to-male ratio of 3:1.

Risk factors

- **Pro-thrombotic Conditions:**

- Factor V Leiden mutation.
- Antithrombin, protein C, and protein S deficiencies.
- prothrombin G20210A mutation
- Antiphospholipid and anticardiolipin antibodies
- Hyperhomocysteinemia

- **Pregnancy & Puerperium**

- **Oral contraceptives:** The most frequent risk factor for CVT in younger female patients

- **Head injury and mechanical precipitants** (e.g., spontaneous intracranial hypotension, lumbar puncture)

- **Infections:**

- Parameningeal infections (e.g., ear, sinus, mouth, face, and neck)
- Systemic infectious disease: bacterial (septicemia, endocarditis, and tuberculosis), viral (measles, hepatitis, herpes simplex, cytomegalovirus, HIV, COVID-19), parasitic (malaria, trichinosis, and toxoplasmosis), and fungal (aspergillosis and cryptococcosis)

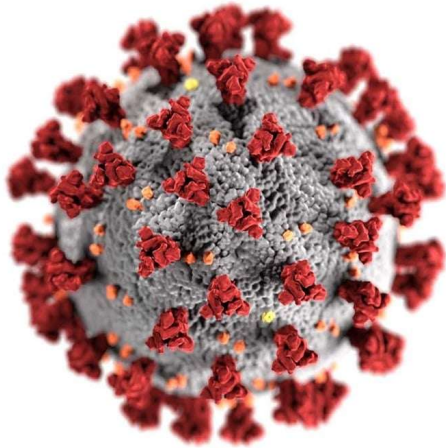
- **Malignancy:**

- Cancer-associated thrombosis (e.g., pancreatic, ovarian, brain, stomach, lung and hematologic cancer).
- Direct invasion by tumors.
- Certain anti-cancer therapies (e.g., tamoxifen, cisplatin, and l-asparaginase)

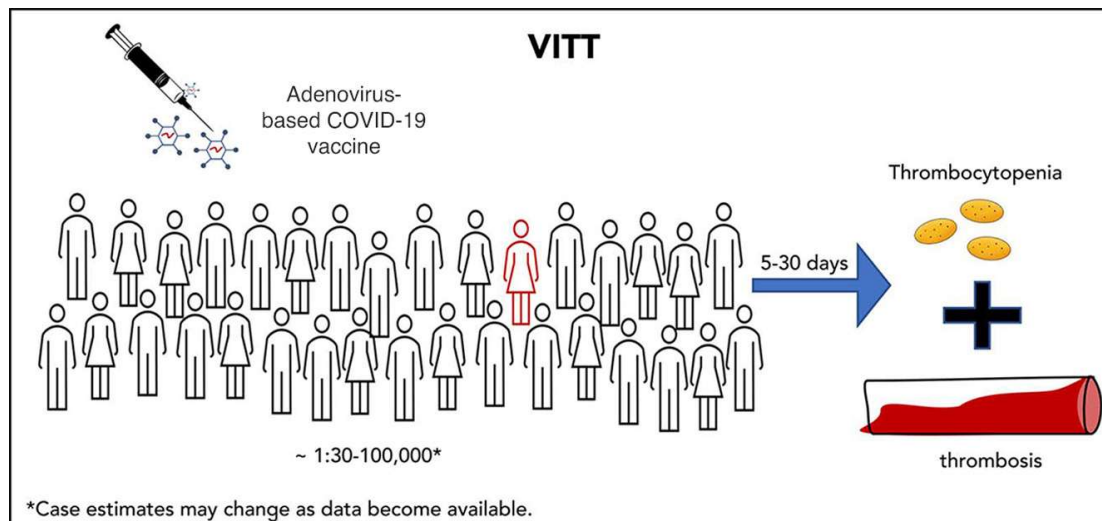
- **Other Factors:**

- Dehydration, especially in infants and young children.
- Inflammatory diseases (e.g., Behçet's disease, inflammatory bowel disease, systemic lupus).
- Immune thrombotic thrombocytopenia (HIT, aHIT, VITT)

COVID-19 and CVT

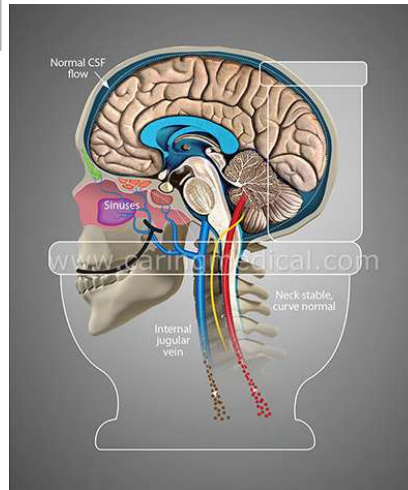
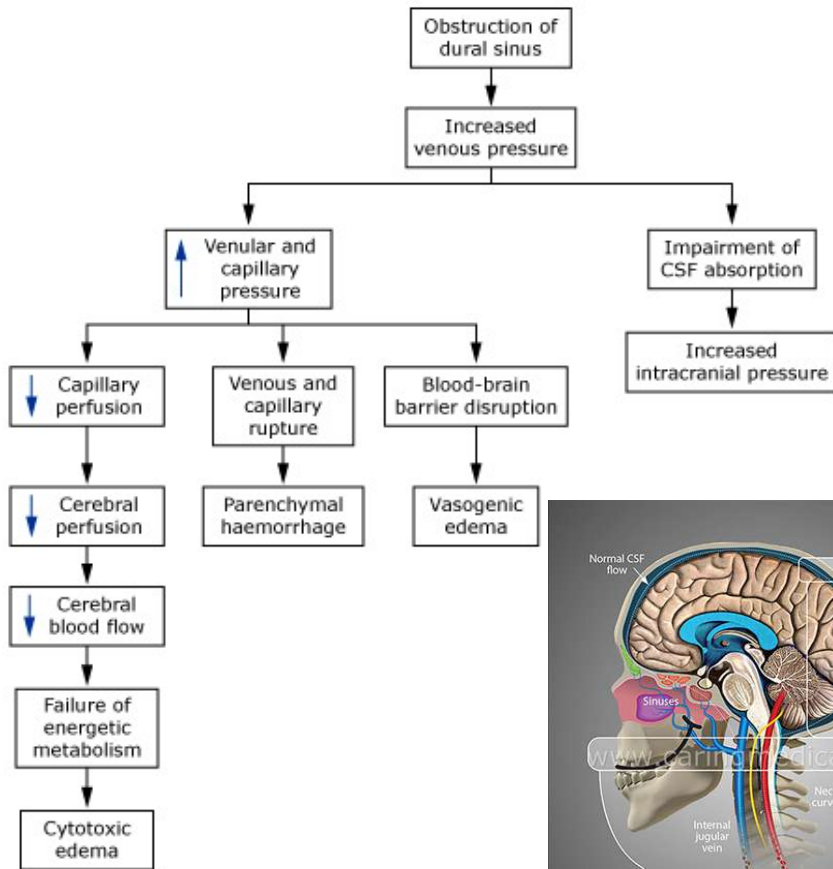


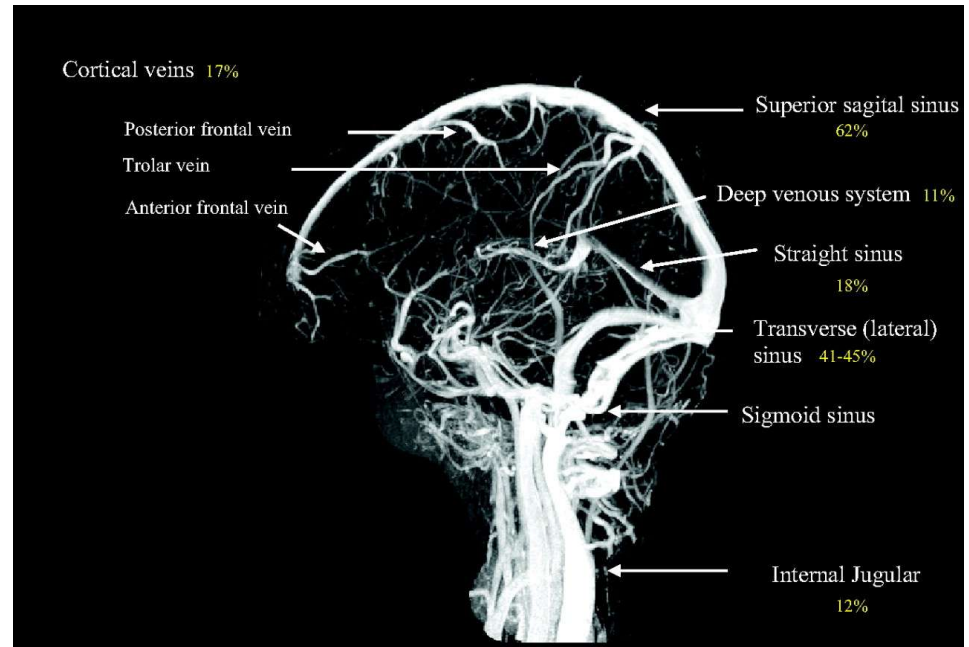
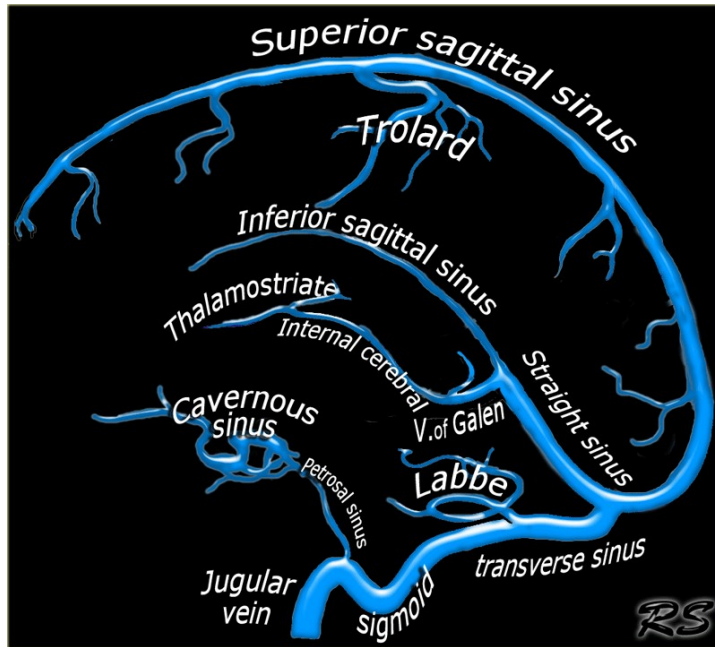
- **Vaccine-induced immune thrombotic thrombocytopenia (VITT): associated with ChAdOx1 nCoV-19 vaccine [AstraZeneca] and Ad26.COV2.S vaccine [Johnson & Johnson/Janssen]**
Immune thrombotic thrombocytopenia mediated by platelet activating antibodies to PF4
 - Heparin-induced thrombocytopenia (HIT)
 - Autoimmune heparin-induced thrombocytopenia (aHIT)
 - Vaccine-induced immune thrombotic thrombocytopenia (VITT)
- **Rare incidence of CVT with SARS-CoV-2 infection: no thrombocytopenia and anti-PF4 antibodies.**



Pathophysiology

- **Venous congestion – increased venular and capillary pressure**
 - Cytotoxic edema
 - Vasogenic edema
 - Parenchymal hemorrhage
 - Cerebral parenchymal lesions (eg, stroke) or seizures
- **Elevated intracranial pressure – impaired CSF absorption**
 - Papilledema
 - Headache
 - Decreased LOC, coma



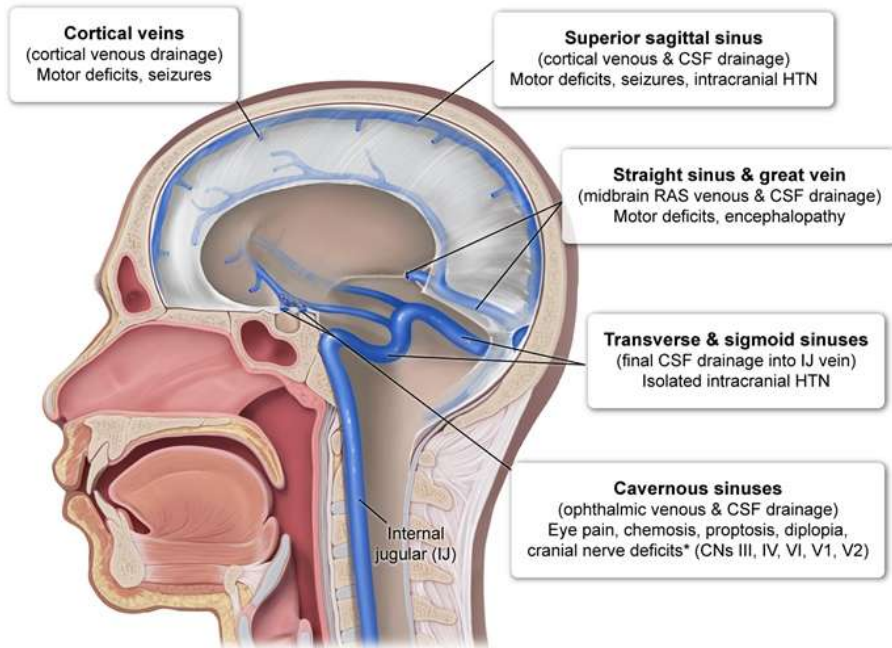


CVT anatomy:

- **Dural sinus thrombosis** → intracranial hypertension
- **Cortical vein thrombosis** → local effects

More than one sinus is involved in over half

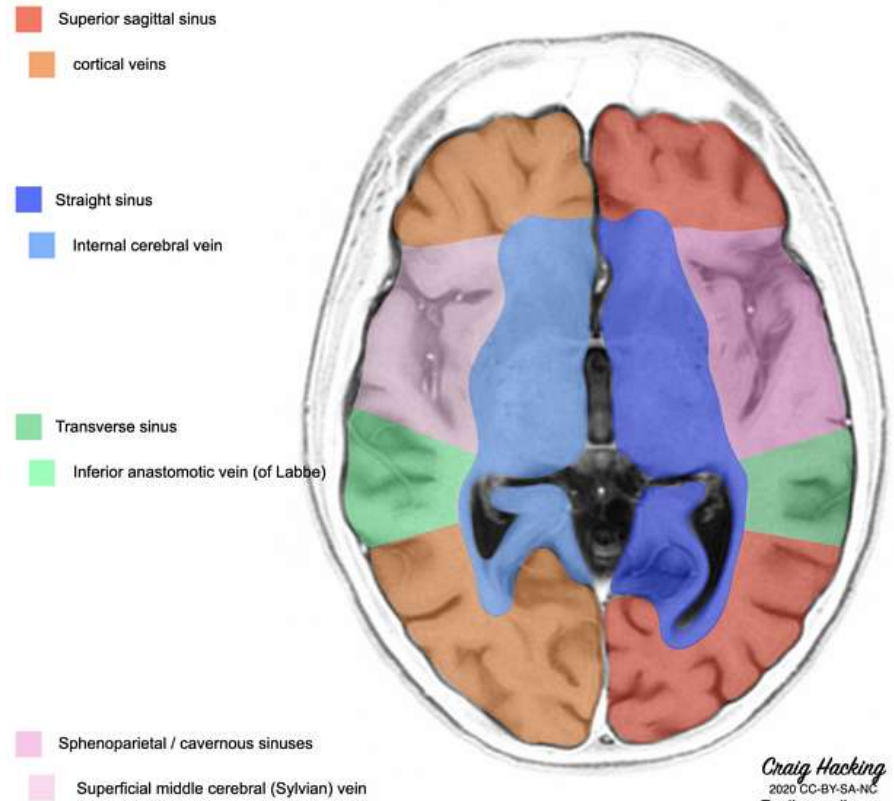
Thrombosis of cerebral veins and venous sinuses



*Due to compression as the cranial nerves pass through the cavernous sinus
CSF = cerebrospinal fluid; HTN = hypertension; RAS = reticular activating system.

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Brain venous vascular territories

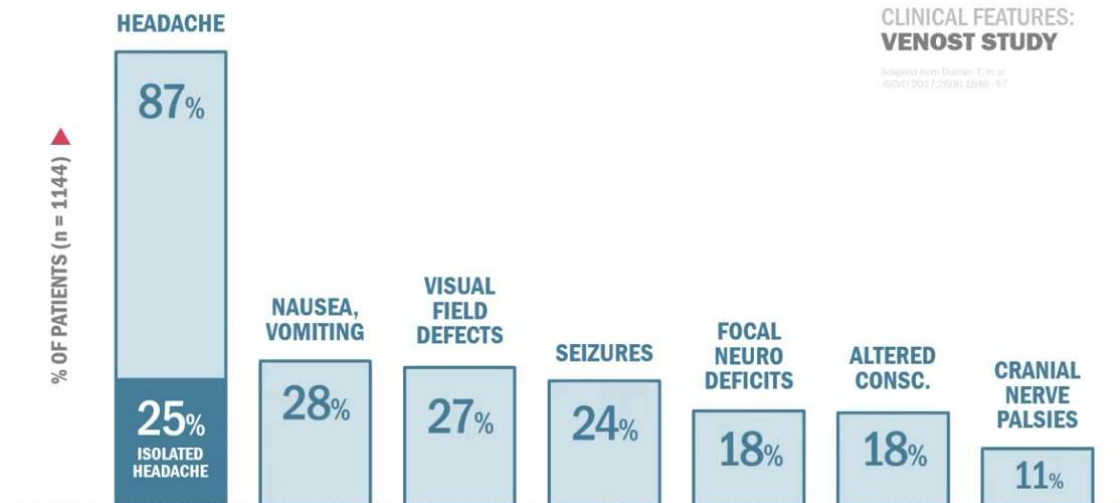


Craig Hacking
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Radiopaedia.org

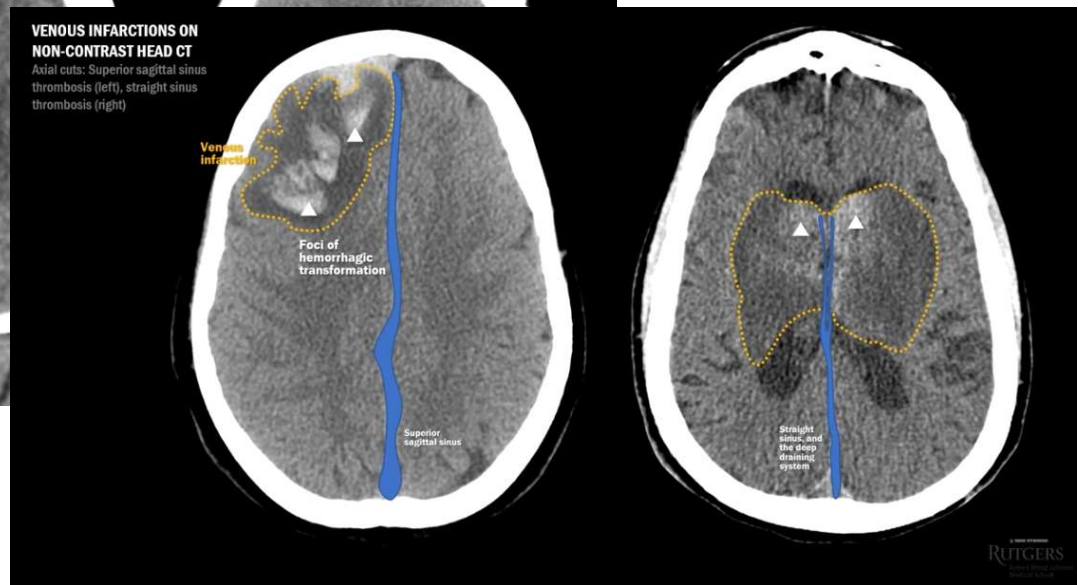
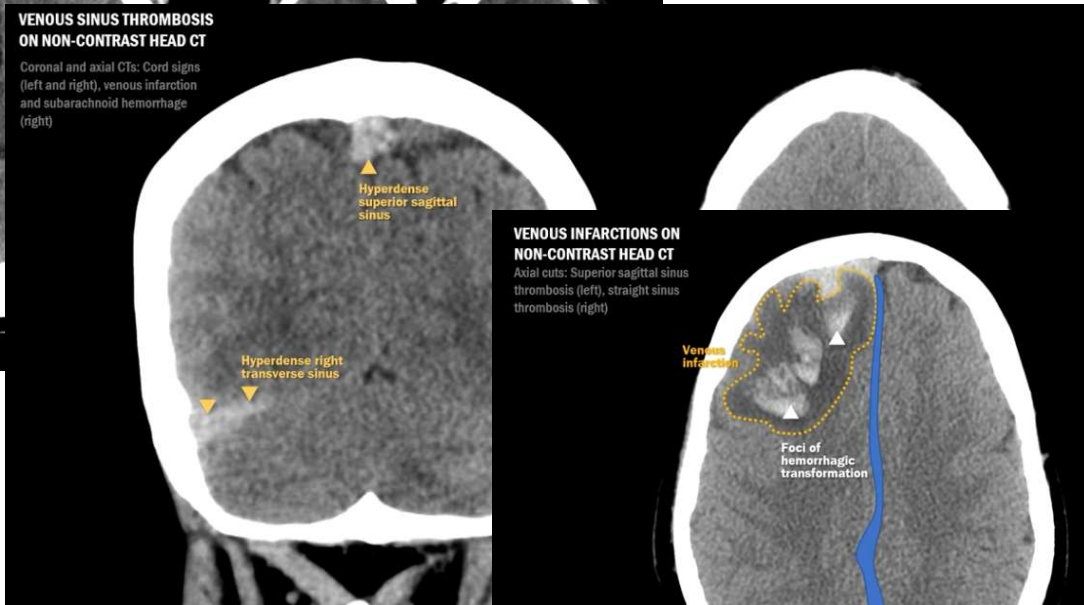
Brain venous vascular territories: <https://radiopaedia.org/cases/80107/studies/93394?lang=us>

Clinical features:

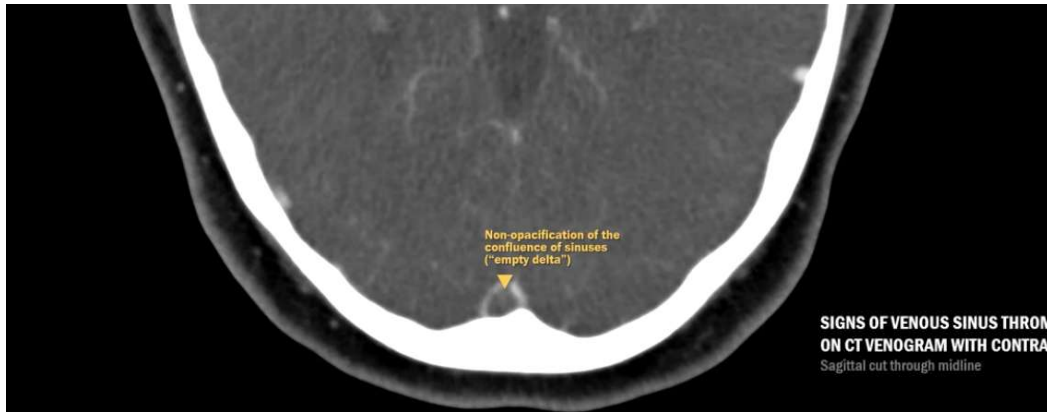
- **Isolated intracranial hypertension syndrome** (headache with or without vomiting, papilledema, and visual problems)
- **Focal syndrome** (focal deficits, seizures, or both)
- **Encephalopathy** (multifocal signs, mental status changes, stupor, or coma)
- **Less common presentations:** cavernous sinus syndrome, subarachnoid hemorrhage, and multiple cranial nerve palsies.



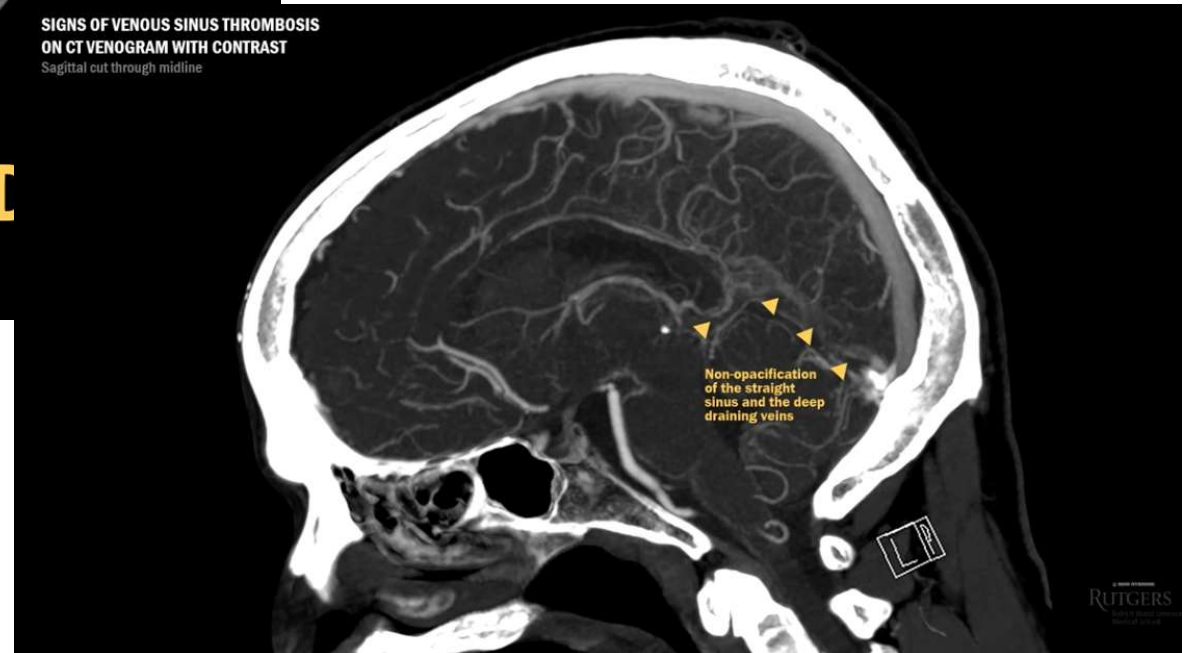
Non-contrast CT head scan: Cord sign, infarction, edema, hemorrhage



CT Venogram (CTV) : Empty-delta sign, non-opacification of sinus and deep veins



SIGNS OF VENOUS SINUS THROMBOSIS
ON CT VENOGRAM WITH CONTRAST
Sagittal cut through midline

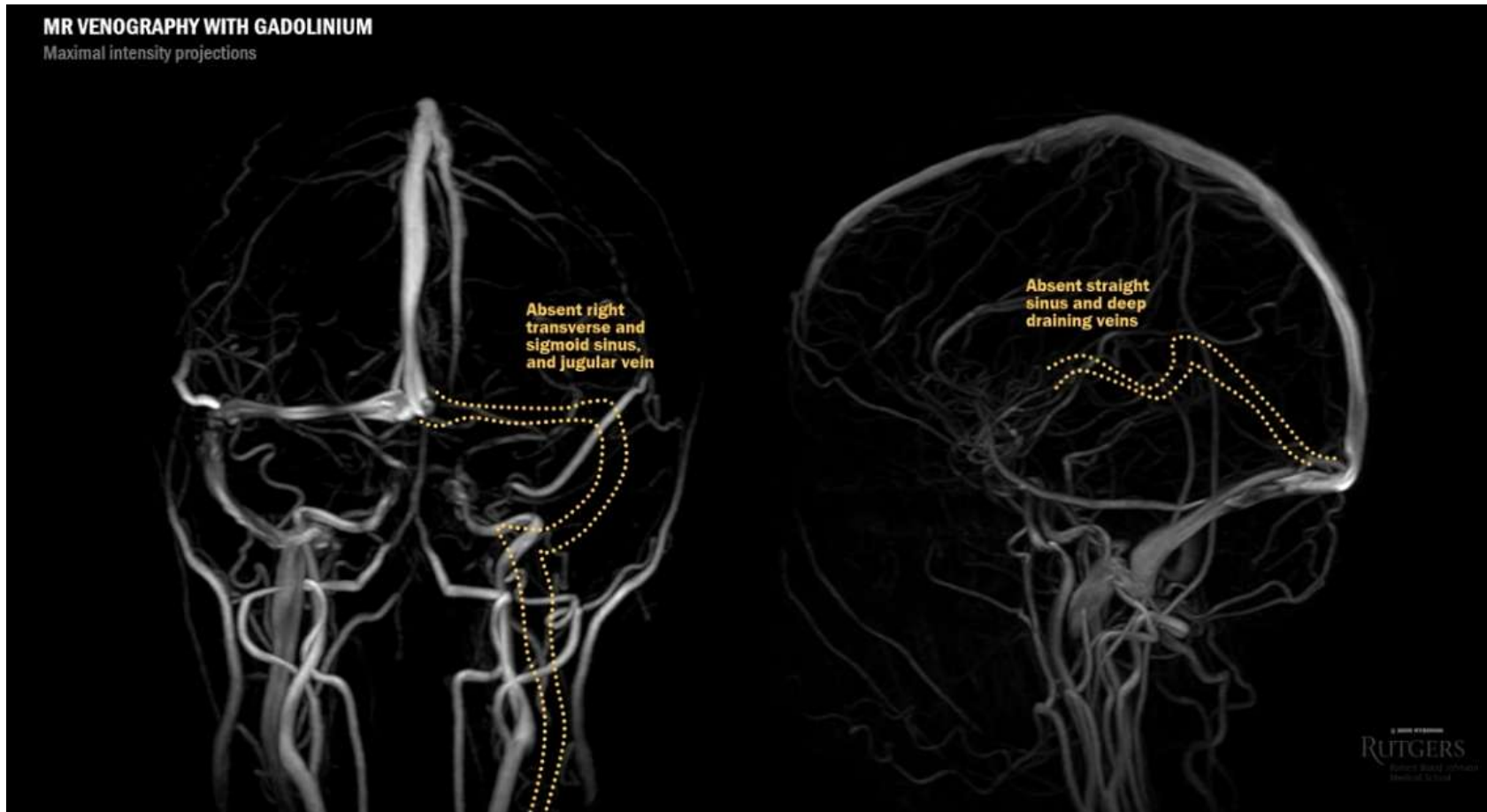


SIGNS OF VENOUS SINUS THROMBOSIS
ON CT VENOGRAM WITH CONTRAST
Axial cut

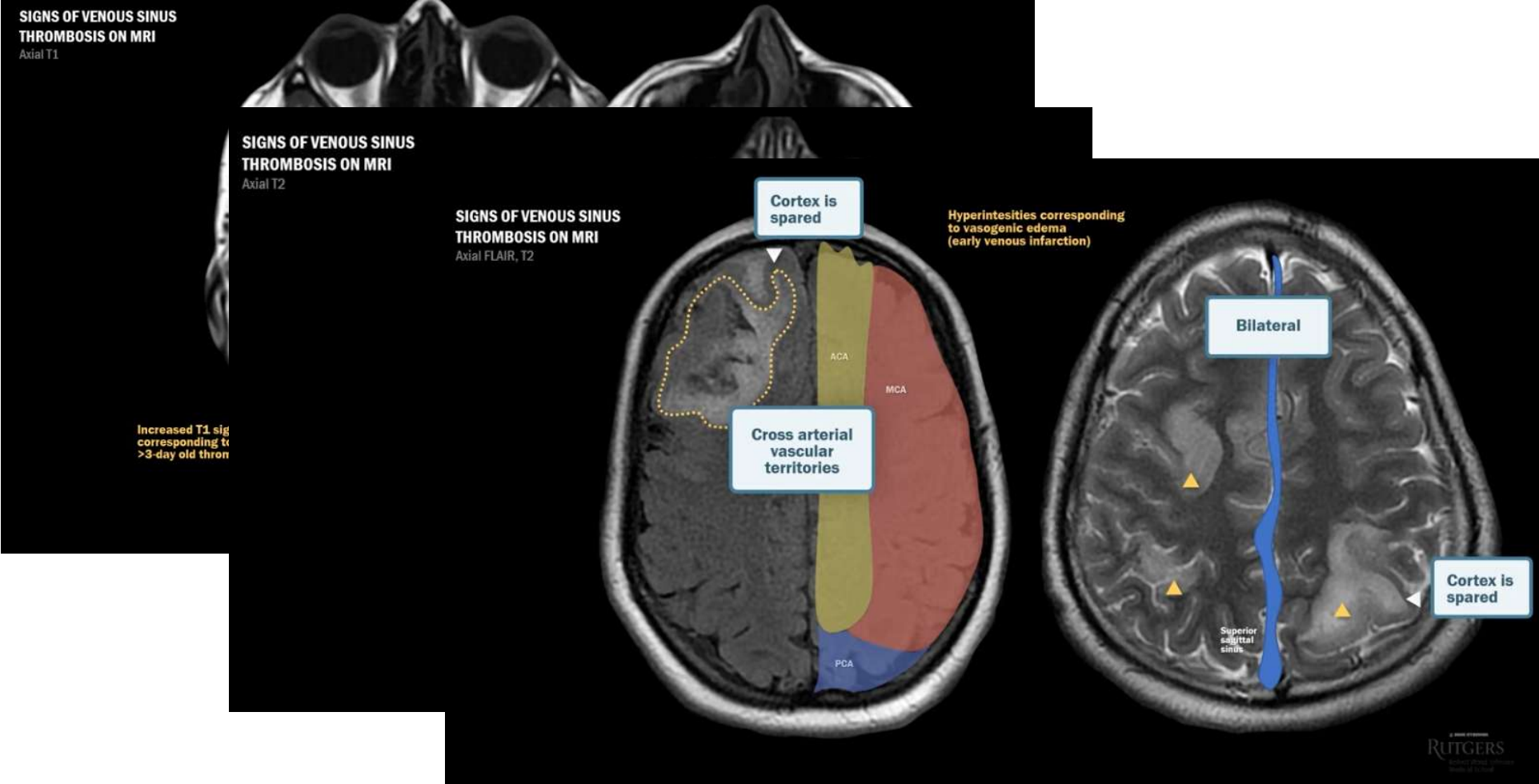
Date courtesy of Sarah D. Radiopaedia.org, #0 14508

Present in
ONE THIRD

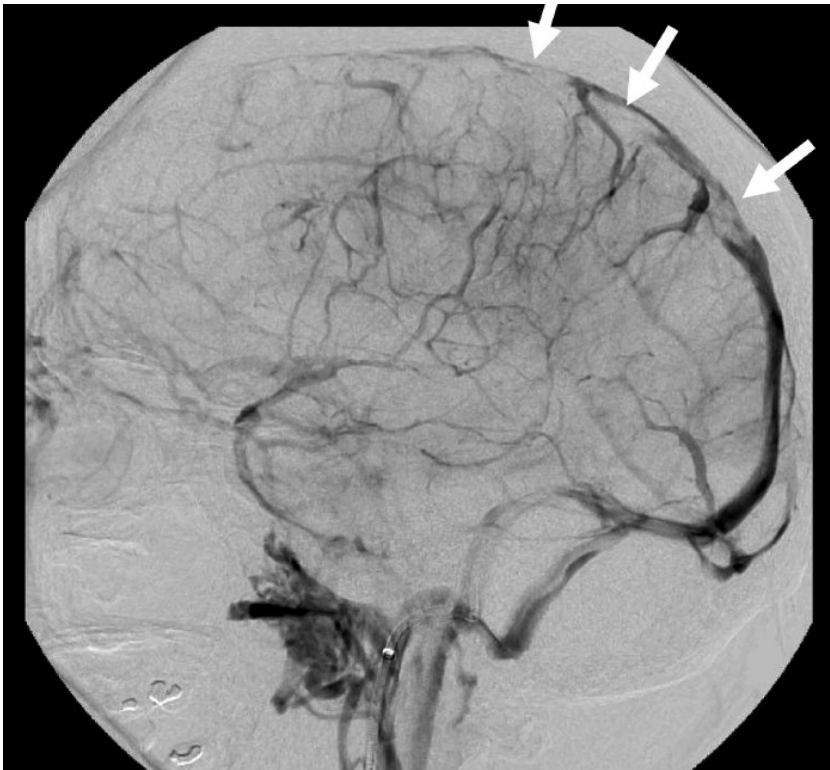
MR Venogram (MRV): absence of sinus and deep veins



MRI: hyperintense (T1) thrombus; absent flow void (T2); infarction

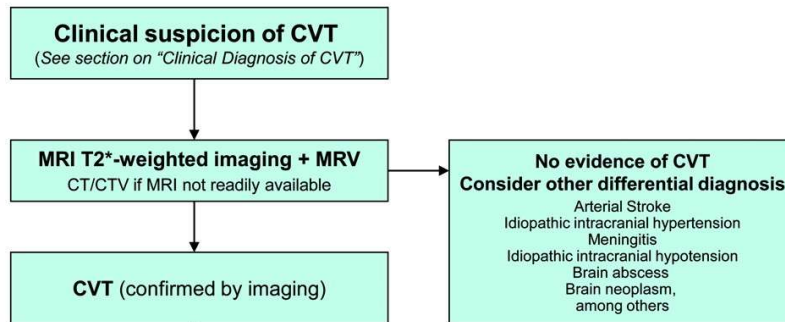


Cerebral Angiography: reserved for situations in which the MRV or CTV results are inconclusive or if an endovascular procedure is being considered.



Guidelines

Proposed Algorithm for the Management of CVT



Initiate anticoagulation (IV heparin or SC LMWH)
if no major contraindications †

Neurological improvement
or stable

Neurological deterioration
or coma despite medical treatment

Continue oral anticoagulation
for 3-12 months or lifelong according
to the underlying etiology
a) Transient reversible factor
b) Low-risk thrombophilia
c) High-risk/inherited thrombophilia
(See section on "Long-Term Management and
Recurrence of CVT")

Severe mass effect or ICH
on repeated imaging

No or mild mass effect
on repeated imaging

May consider decompressive
hemicraniectomy
(lifesaving procedure)

May consider endovascular
therapy (with or without
mechanical disruption) ‡

All patients should receive support for the prevention of complication and symptomatic therapy
(eg, management of seizures, intracranial hypertension)


AHA/ASA Scientific Statement

Diagnosis and Management of Cerebral Venous Thrombosis A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

*The American Academy of Neurology affirms the value of this statement as
an educational tool for neurologists.*

Gustavo Saposnik, et al. Stroke. 2011;42:1158-1192

European Stroke Organization guideline for the diagnosis and
treatment of cerebral venous thrombosis – endorsed by the European
Academy of Neurology

J. M. Ferro^{a,b}, M.-G. Bousser^c, P. Canhão^{a,b}, J. M. Coutinho^d, I. Crassard^c, F. Dentali^e, M. di Minno^{f,g},
A. Maino^h, I. Martinelli^h, F. Masuhrⁱ, D. Aguiar de Sousa^a  and J. Stam^d, for the European Stroke Organization

J. M. Ferro, et al. European Journal of Neurology. 2017, 24: 1203–1213

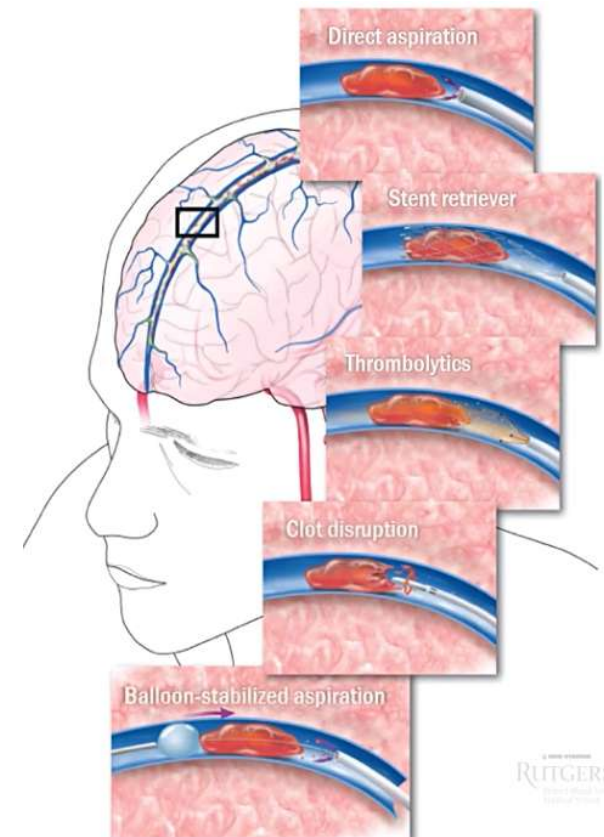
Treatment and management:

• Anticoagulation therapy:

- **Initial anticoagulation:** IV Heparin or SC LMWH, even if there is hemorrhagic infarction.
 - ESO guidelines have a weak recommendation for LMWH over unfractionated heparin
- **Transition to oral anticoagulants:** Warfarin or direct oral anticoagulants (DOACs)
 - RESPECT-CVT: dabigatran vs warfarin (comparable outcomes)
 - Ongoing clinical trials: SECRET (Study of Rivaroxaban as initial therapy for CVT)
- **Duration** varies, typically 3-12 months or longer.
 - Patients with provoked CVT: a 3 to 6 month
 - Patients with unprovoked CVT: 6 to 12 months
 - Patients who have recurrent venous thrombosis or prothrombotic condition: may need permanent anticoagulation
 - Ongoing clinical trials: EXCOA-CVT (3 to 6 versus 12 months)
- **VITT:** avoid heparin, treatment with non-heparin anticoagulant, DOACs, or plasma exchange, IVIG

• Endovascular therapy

- For severe or worsening cases despite anticoagulation (mental status disorder, coma state, intracerebral hemorrhage, or thrombosis of the deep venous system)
- For patients with contraindication to anticoagulation
- TO-ACT trial: terminated early for futility



Prognosis

- The prognosis for CVT is generally better than that of arterial strokes. With appropriate treatment, many patients recover without residual symptoms.
- Mortality: in-hospital mortality rate ranging 1%-4%, 8%-10% during long-term follow-up.
- Complete recovery: 79% (mRS score <2)
- High rate of venous recanalization: around 85%
- Recurrence rate is low: 2%-3% had recurrent sinus thrombosis
- Neuropsychological sequelae: over 50% of survivors feel depressed or anxious, and minor cognitive or language deficits.

Table 6. Variables Associated With Poor Prognosis in Cohort Studies

Demographic	Clinical	Neuroimaging	Risk Factors
Age >37 y ¹⁰	Coma ^{10,117,277}	Intracerebral hemorrhage ^{10,277}	Cancer ^{10,177}
Male sex ¹⁰	Neurological deficit and severity (NIHSS) ^{177,179}	Involvement of the straight sinus ²⁷⁷	CNS infection ¹⁰
	Encephalopathy ¹¹⁷	Thrombosis of the deep venous system ¹⁰	Underlying coagulopathy hereditary thrombophilia ⁶⁶
	Decreased level of consciousness ¹⁰		
	Hemiparesis ¹⁰	Venous infarction ^{66,179}	
	Seizures ^{10,179}		

NIHSS indicates National Institutes of Health Stroke Scale; CNS, central nervous system.

Reference

- Saposnik, et al. Diagnosis and Management of Cerebral Venous Thrombosis. *Stroke*. 2011;42:1158-1192.
- J. M. Ferro, et al. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – endorsed by the European Academy of Neurology. *European Journal of Neurology* 2017, 24: 1203–1213
- Allan H. Ropper, Joshua P. Klein. Cerebral Venous Thrombosis. *N Engl J Med* 2021;385:59-64.
- Faisal Khan, Neha Sharma, Moin Ud Din and Ryan Chetram. Diagnostic and Therapeutic Challenges of Cerebral Venous Thrombosis in SARS-CoV-2 Infection: A Case Report and Review of Literature. *Clin. Pract.* 2021, 11, 598–606.
- Ferro J. et al. *JAMA Neurol.* Safety and Efficacy of Dabigatran Etxilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis A Randomized Clinical Trial. 2019; 76 (12): 1457-1465
- Mohamad Abdalkader, et al. Cerebral venous disorders: Diagnosis and endovascular management. *Journal of Neuroradiology* 000 (2023) 1–12.
- Ferro JM, Coutinho JM, Dentali F, et al. Safety and efficacy of dabigatran etexilate vs dose-adjusted warfarin in patients with cerebral venous thrombosis: a randomized clinical trial. *JAMA Neurol* 2019;76(12):1457–1465.
- Field T, Dizonno V, Hill M. Ongoing clinical trials: study of rivaroxaban for Cerebral venous thrombosis (SECRET). *Int J Stroke* 2019;14(3)3–52.
- Miranda B, Aaron S, Arauz A, et al. The benefit of Extending oral anticoagulation treatment (EXCOA) after acute cerebral vein thrombosis (CVT): EXCOA-CVT cluster randomized trial protocol. *Int J Stroke Off J Int Stroke Soc* 2018;13(7):771–774.
- Richard J Perry, Arina Tamborska, et al. Cerebral venous thrombosis after vaccination against COVID-19 in the UK: a multicentre cohort study. *Lancet* 2021; 398: 1147–56.
- Taskin Duman, et al. A multicenter study of 1144 Patients with cerebral venous thrombosis: The VENOST study. *Journal of Stroke and Cerebrovascular Diseases*, Vol. 26, No.8 (August), 2017: pp 1848–1857
- Mohammad Saadatnia, et al. Cerebral venous sinus thrombosis risk factors. *World Stroke Organization International Journal of Stroke* Vol 4, April 2009, 111–123
- Igor Rybinnik MD. Diagnosis and Management of Cerebral Venous Thrombosis. https://www.youtube.com/watch?v=iQsXCqL_OeM
- Brain venous vascular territories: <https://radiopaedia.org/cases/80107/studies/93394?lang=us>



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Thank you!