Chapter

Cerebral Veins and Dural Sinuses Thrombosis: State-of-the-Art Diagnosis

Dragos Catalin Jianu, Silviana Nina Jianu, Nicoleta Iacob, Traian Flavius Dan, Georgiana Munteanu, Anca Elena Gogu and Ligia Petrica

Abstract

Cerebral veins and dural sinus thrombosis (CVT) represents a rare cause of stroke. In adults, CVT has a higher frequency among cases with inherited thrombophilia, mostly women, patients with malignancy, or infections. Two pathophysiological mechanisms contribute to their clinical presentation: diminution of cerebrospinal fluid absorption and increase of venular and capillary pressure. Four major syndromes have been described as isolated or in combination: intracranial hypertension, focal neurological deficits, seizures, and encephalopathy. Non-enhanced CT (NECT) of the head is the most frequently performed imaging study in the emergency department. Features of CVT on NECT can be divided into direct signs (detection of venous clot within a venous channel) and, more frequently, indirect signs (such as cerebral edema or cerebral venous infarct). CVT diagnosis is confirmed with CT venography, which can be performed immediately after NECT, and detects the venous clot as a filling defect, or magnetic resonance imaging (MRI)/MR venography. Different imaging techniques may need to be combined to avoid pitfalls. Conclusions: CVT is a relatively rare disorder in the general population and due to its wide clinical spectrum is frequently misdiagnosed upon initial examination. The knowledge of variable clinical aspects and imaging signs will be essential in providing a timely diagnosis.

Keywords: cerebral veins and dural sinuses thrombosis (CVT), thrombophilia, headache, non-enhanced computed tomography (NECT) of the head, computed tomography (CT) venography, magnetic resonance imaging (MRI) of the head, magnetic resonance (MR) venography

1. Introduction

Cerebral veins and dural sinuses thrombosis (CVT) is a rare disease in the adult population, with a significant higher frequency among cases with inherited (genetic) thrombophilia, and young patients, especially women (due to their peculiar acquired

prothrombotic conditions, such as pregnancy, puerperium, or oral contraceptive therapy) [1–5].

Unfortunately, because of its frequently misleading clinical presentation associated with the overlapping signal intensities of acute thrombosis and venous flow on conventional magnetic resonance (MR) images and MR venograms, CVT is difficult to diagnose [6–8].

CVT patients rarely appear as an arterial stroke syndrome, with an acute onset of focal neurological deficits associated with classic vascular risk factors [1–5]. Different imaging techniques are essential in precisely detecting cases with clinically suspected CVT [5–7].

Our chapter will present the cerebral veins and dural sinuses anatomy, the epidemiology, etiology, pathophysiology, and clinical and imagistic aspects of CVT [7–9].

2. Cerebral veins and dural sinus anatomy

Venous blood from the brain is drained by the cerebral veins into the intracranial dural sinuses. Familiarity with their anatomic variants or anomalies is mandatory to accurately diagnose CVT.

2.1 Cerebral veins anatomy

They consist of three groups: the cortical veins, the deep cerebral veins, and the posterior fossa veins (**Figure 1**) [3, 10]. The cerebral veins present different aspects that can determine different features of CVT: on one hand, the superficial, and the posterior fossa veins have extensive anatomic inconsistency (in number, side, and anastomoses), therefore proving why the digital substraction angiography (DSA) detection of their isolated thrombosis is problematic (with the absence of distinct cortical or posterior fossa venous territories and a misleading clinical spectrum); on the other hand, the thrombosis of the deep cerebral veins is clear to diagnose at angiography, because these

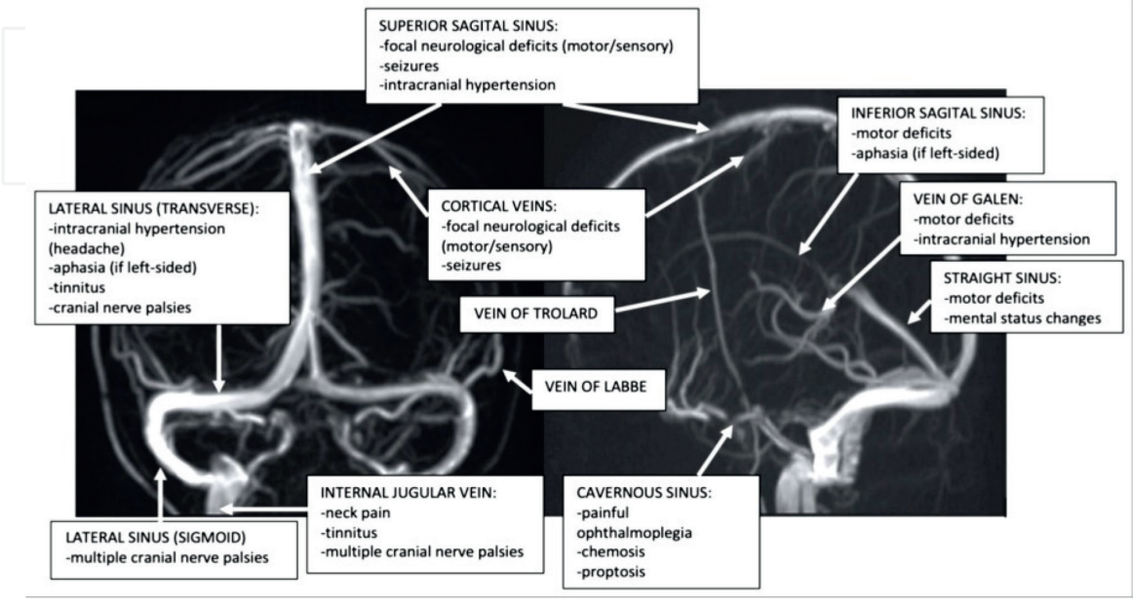

Figure 1.
Cerebral venous channels anatomy and main clinical spectrum according to the location of CVT.

veins (except for the anatomic variants of the veins of Rosenthal) are constant, always having distinct venous territories and clinical aspects, respectively [3, 10].

The cerebral veins possess thin walls and, without a muscular tunic, present no valves, with different anastomoses, which determine both their dilatation and the inversion of venous flow toward the brain if there is a thrombosis of the sinus into which they drain [3, 10].

2.2 Dural sinuses anatomy

The intracranial dural sinuses consist of a system of interconnected multiseptated endothelium-lined channels without valves, situated between the periostal and meningeal dural layers. Their walls are represented by the outer and inner fibrous leaves of the dural mater. Inside them are situated the arachnoid villi and Pacchioni's granulations, which have an important role in the cerebrospinal fluid (CSF) resorption, especially at the level of the superior sagittal sinus (SSS) and lateral sinus (LS), in which most of the CSF absorption unfolds [3, 10].

The dural sinuses are represented by two groups: the posterior-superior, and the antero-inferior (**Figure 1**).

The first group comprises the SSS, inferior sagittal sinus (ISS), LS (consisting of transverse sinus and sigmoid sinus), straight sinus (SS), and occipital sinus. The torcular Herophili is the junction of SSS, SS, transverse sinus, and occipital sinus. The second group includes the cavernous sinus, and the superior and inferior petrosal sinuses. Sometimes, the anterior portion of the SSS is narrow (hypoplasia) or with aplasia or even replaced by two frontal veins, which unite at the level of the coronal suture (explaining why its isolated lack of filling at angiography it is not enough to affirm its occlusion by the venous clot). Another variant consists of a duplication of SSS posterior portion [3, 10, 11].

Frequently (in 50–80% of the cases), the two transverse sinuses are asymmetric; usually, the right transverse sinus is larger than the left (in these cases being a direct continuation of the SSS), so an isolated lack of filling of the transverse portion of the LS is usually suggestive of hypoplasia, or aplasia of the posteromedial segment of the left transverse sinus, not of thrombosis.

The cerebral veins empty especially posteriorly, from the SSS or the SS into the LSs, and only a minority drain anteriorly, to the cavernous sinuses [3, 10].

The dural sinuses empty into the two internal jugular veins, for the horizontal position, and into the vertebral veins for the standing position. In order to avoid venous blood going back upward to the brain in cases of augmented intra-thoracic pressure, IJV present valves [12].

3. Epidemiology

Unfortunately, no epidemiologic studies of CVT contain the essential criteria for an accurate epidemiologic stroke study, due to different aspects, including the multiple nonspecific clinical features of CVT [8, 13, 14].

Current data denote that CVT is an uncommon disease, only less than 0.5–1% of all strokes [14], with a prevalence higher than previously considered, due to a raised awareness of CVT among different clinicians, and a higher accessibility to modern imaging techniques, such as MRI/MR Venography, for the assessment of ambiguous clinical aspects, such as headache and seizures [8, 13–16].

The estimated incidence of CVT ranges from 1.16 to 2.02 per 100,000 inhabitants [13]. According to different studies, CVT is more frequent in children than in adults, occurring infrequently in cases older than 65 years [8, 9]. The peak incidence in adults' population is in their third decade; thus, CVT tends to present at a younger age than those with arterial types of strokes [8]. The median age in the prospective International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) cohort was 37 years [7], and only 8% of the cases presented more than 65 years old [17].

CVT has prominent differential sex prevalence only in adults, being sex-independent in children and the elderly. In the 624 adult patients of ISCVT cohort, there was observed a women predominance (3:1); this imbalance is the consequence of an augmented risk of CVT in women, attributed to a sex-specific risk factor/prothrombotic condition (i.e., oral contraceptives, abortion, pregnancy, puerperium, or hormone replacement therapy) [8, 9].

4. Etiology-risk factors

There are numerous predisposing risk factors for CVT, including all factors that determine the composition of blood, especially those that can induce an alteration in the vascular endothelium or blood stasis [9].

According to ISCVT, the most frequent risk factors observed in elderly cases with CVT are thrombophilia and malignancy [17, 18].

In the Canadian pediatric ischemic stroke registry, thrombophilia was noted in 41% of all cases. Other risk factors were infections, connective tissue diseases, and neoplasms [19].

In adult patients of the ISCVT cohort, in 85% of cases, at least one risk factor was detected, and in about half of CVT cases, two or more risk factors were identified; in consequence, the detection of a first risk factor should not stop a search for possible others [9]. A prothrombotic condition was noted in one-third of all cases of the ISCVT cohort, and genetic thrombophilia was reported in 22% of all CVT cases [9]. The most frequent risk factors identified in adults with CVT are genetic thrombophilia, oral contraceptives (OC), pregnancy, puerperium, and neoplasms [9, 14].

4.1 Thrombophilia

4.1.1 Genetic (inherited) thrombophilia

In thrombophilia appears an overactivity of procoagulant factors or a deficiency in anticoagulants factors, leading to thrombus formation.

The main genetic thrombophilia as inherited procoagulant conditions for CVT are represented by: factor V Leiden (FVL) pathologic variant (activated Protein C resistance) [19–22]; G20210 A prothrombin gene pathologic variant [19, 22–24]; and hyperhomocysteinemia [25].

In a meta-analysis of case-control studies, the prevalence of FVL variant between patients' group and controls group was 12.8% versus 3.6%, and carriers of the FVL variant were more likely to develop CVT (odds ratio [OR] 3.1, 95% CI 1.8–5.5) [26]. In this meta-analysis, the authors observed that the prevalence of the G20210 A prothrombin gene pathologic variant between the patients group and the controls group was 5.2% versus 2.5%, and carriers were suggestively more likely to present the disease (OR 3.1, 95% CI 1.4–6.8) [26].

The possible connection between hyperhomocysteinemia produced by some inherited variants in methylenetetra-hydrofolate reductase (MTHFR) with CVT is still debated [20, 23, 26]. Gouveia and Canhão noted that the occurrence of the MTHFR 677C > T polymorphism in adult cases was comparable for 382 patients presenting CVT versus 1217 subjects from the control group (15.7% vs. 14.6%; OR 1.12, 95% CI 0.8–1.58). They concluded that the MTHFR 677C > T polymorphism does not represent a risk factor for CVT [27]. Marjot et al. observed in a meta-analysis, that the MTHFR 677C > T polymorphism was associated with CVT [OR 2.30, 95% CI 1.20–4.42) [20, 28]. There is no association of CVT with PAI-1 [8, 29].

The anticoagulant factors that regulate thrombin include: antithrombin, protein C, and protein S; thus, the main genetic thrombophilia as inherited anticoagulant conditions for CVT is represented by antithrombin deficiency [30], and protein C or protein S deficiencies [18, 31].

4.1.2 Acquired thrombophilia

The most frequent acquired thrombophilia observed in CVT is due to pregnancy, puerperium, OC, malignancy, and obesity [32, 33]. For example, in the ISCVT cohort of 624 adults with CVT, a sex-specific risk factor was detected in 65% of women, which represented 75% of all adult cases [9].

4.2 Pregnancy and puerperium

On one hand, in high-income countries, pregnancy and puerperium are risk factors in 5–20% of all CVT cases [9]. On the other hand, in low-income countries, puerperium is the main risk factor for CVT, with about 30% of all cases [34–37]. Usually, CVT is observed in the third trimester or in the first 3 weeks after delivery, due to the hypercoagulability state and the venous stasis that are noted during this period of time [34–37]. Pelvic phlebothrombosis may generate CVT *via* the venous plexuses of the vertebral channel, and the basilar venous plexus [34–37].

4.3 Therapy with estrogens, such as hormonal oral contraceptives (OC) or replacement therapy

According to different studies, the most frequent risk factor for CVT in younger women is represented by the use of OC [38, 39]. OC may be the single identified risk factor, or may be associated with other risk factors for CVT, such as vasculitis (especially systemic lupus erythematous or Behçet's disease), obesity [40], or inherited thrombophilia; in this last association, the risk of intra-, or extracerebral thrombosis is six times higher than that of nonusers of OC [9, 41]. A few case reports observed the association between tamoxifen (an estrogen receptor modulator) and CVT [42].

In contrast to genetic thrombophilia, pregnancy and OC are transient risk factors for CVT and they are not related to a higher risk for recurrence [34–37].

4.4 Obesity

Obesity represents a risk factor for CVT and different types of venous thromboembolism. In an observational study of 186 cases with CVT and matched controls, obesity was linked with an augmented risk of CVT for women (adjusted odds ratio

[aOR] 3.5, 95% CI 2.0–6.1) but not men (aOR 1.2, 95% CI 0.3–5.3). The risk was maximum for obese women consuming OC (aOR 29.3, 95% CI 13.5–63.6) [40].

4.5 Neoplasms

In the ISCVT cohort, malignancy was 7.4% of all CVT patients [7]. The most frequent cancers related to CVT are different solid tumors outside the Central Nervous System (CNS) (such as breast tumors or medullary carcinoma of the thyroid), hematologic neoplasms, and CNS malignancies (like medulloblastoma) [14]. The most important pathophysiological mechanisms are represented by direct tumor compression or invasion of dural sinuses, leukostasis, and hypercoagulability, which is determined by increase in acute-phase reactants, or modified coagulation factors from chemotherapy (L-asparaginase, cisplatin), or hormonal drugs [8, 14].

4.6 Hematologic disorders

Different Philadelphia-negative myeloproliferative neoplasms (MPNs) (including polycythemia Vera–PV, essential thrombocythemia, and primary myelofibrosis) develop an increased risk of venous thrombosis. However, previous studies observed that CVT is rarely associated with MPNs (especially PV). PV is a BCR:ABL1 negative, chronic MPN defined by the uncontrolled proliferation of erythroid mass due to an abnormal clone of hematopoietic stem cells, leading to an augmentation in hemoglobin and hematocrit levels and can be associated with an increase in the appearance of myeloid leukocyte cells and megakaryocytes. The Janus kinase 2 V617F (JAK2V617F) mutation led to the diagnosis of PV [17]. Other hematological disorders that can produce CVT are paroxysmal nocturnal hemoglobinuria, heparin-induced thrombocytopenia, and thrombotic thrombocytopenic purpura [14].

4.7 COVID-19 infection and COVID-19 vaccine-associated

4.7.1 CVT COVID-19 infection-associated CVT

Different cases of CVT have been reported in patients with SARS-CoV-2 infection, this type of infection being the only identified risk factor [43, 44]. According to the European Medicines Agency safety committee report concerning 34,331 cases hospitalized with SARS-CoV-2 infection, the frequency of CVT was very low 0.08% (95% CI 0.01–0.5), but with an alarming in-hospital death of 40% [45].

4.7.2 COVID-19 vaccination-associated CVT

Vaccine-induced immune-mediated thrombocytopenia (VITT) is an unusual type of thrombosis linked with thrombocytopenia, commonly determining CVT, and splanchnic vein occlusion, that has been identified subsequently to adenovirus vector vaccines against COVID-19: ChAdOx1 nCOV-19 (AstraZeneca) and Ad26.COV2-S Johnson and Johnson (Janssen/J&J) [46]. Even if there have been reported some cases of CVT subsequently to mRNA vaccines, they did not present the aspects of VITT and could have been incidental [47].

According to Perry et al. [47], when they are compared with those without VITT, cases with VITT-associated CVT were younger, had fewer associated other venous

thrombosis risk factors, and were vaccinated with the ChAdOx1 vaccine. They presented extensive CVT with multiple cerebral veins and dural sinuses thrombosed, and multiple intracerebral hemorrhages. These CVT patients were more likely to present simultaneously splanchnic veins or arterial thromboses. Their outcomes at discharge were worse, with significantly higher rates of death and disability (22–47%), compared with those with other causes of CVT (3–5%) [47, 48]. The main diagnostic criteria for definite VITT-associated CVT are represented by post-vaccine CVT (4–28 days after COVID-19 vaccination), thrombocytopenia, and anti-platelet factor 4 antibodies (anti-PF4 antibodies) [47–49].

4.8 Infections

In the past, different loco-regional or systemic infections were the main etiology of CVT. Actually, in developed countries (especially due to higher accessibility to antibiotics) septic thrombosis of cerebral veins and dural sinuses (cerebral thrombophlebitis) in adults has become an unusual type of CVT (6–12%), but sometimes with significantly higher rates of death and disability [9, 32]. In developing countries, infections represent an important etiology of CVT (18% of cases) [36]. Acute infections of the middle third of the face (especially with *Staphylococcus aureus*), different paranasal sinusitis, multiple dental abscesses, otitis media, mastoiditis, or different infections of throat or scalp can determine acute cerebral thrombo-phlebitis, especially for the cavernous and lateral sinuses. Chronic CVT is produced especially by gram-negative germs or by fungi (Aspergillus). Cerebral thrombophlebitis may also develop as a complication of other loco-regional infections, such as meningitis, epidural, or brain abscesses, or after different open traumatic injury of the head, pelvic phlebothrombosis, or even after systemic infections (trichinosis, cytomegalovirus) [3].

4.9 Systemic autoimmune diseases

The most frequent are systemic lupus erythematosus (SLE), with or without the nephrotic syndrome, Behçet disease, and inflammatory bowel disease [8, 14].

4.10 Head injury and mechanical precipitants

These are rare causes of CVT.

a. Cerebral veins and dural sinuses could be occluded by different loco-regional factors, such as head trauma, brain tumors, arachnoid cysts, arteriovenous malformations, and by

b. Mechanical factors, such as neurosurgical procedures, lumbar puncture, jugular venous cannulation, epidural blood patch, or spontaneous intracranial hypotension [3, 50].

4.11 Cryptogenic (idiopathic) CVT

There is still a minority of CVT cases with no underlying etiology or risk factor. Thus, in the ISCVT cohort, no risk factors could be determined in about 13% of CVT adult cases [9], in a higher percentage for older patients (37%) [9, 17], and in a lower percentage for children (only 10%), respectively [19].

5. Pathophysiology

The pathophysiology of CVT is still incompletely known, due to multiple reasons, including different anatomic variants or anomalies of the cerebral venous channels and the paucity of experiments in animal models of CVT [9]. However, there are two pathophysiological mechanisms determined by the thrombosis of cerebral veins and dural sinuses; they are represented by the diminution of cerebrospinal fluid (CSF) absorption, and by the increase of venular and capillary pressure, respectively (**Figure 2**) [5, 51–53].

5.1 The diminution of CSF absorption in CVT cases

It is generated by the occlusion of the dural sinuses.

The normal absorption of CSF occurs in the arachnoid granulations and glymphatic system, which drains CSF into the dural sinuses, especially at the level of the SSS, LS, and internal jugular vein (IJV). In the case of dural sinuses thrombosis, a rise of the venous pressure occurs, with a consecutive decrease of CSF absorption which, secondary, elevates the intracranial pressure. This phenomenon determines an increase in venular and capillary pressure and produces vasogenic and cytotoxic edema and cerebral hemorrhage [5, 51–53].

5.2 The increase of venular and capillary pressure

It is the result of the obstruction of different dural sinuses and cerebral veins [5, 51–53].

In the initial stages of venous occlusion, a decreased but still efficient perfusion of the corresponding brain territory might be possible, due to the dilatation of cerebral veins (which present thin walls, without a muscular tunic) and, to the recruitment of efficient collateral pathways: veins of Troland and Labbe (because the cerebral veins present no valves, with the subsequent inversion of venous flow toward the brain if there is thrombosis of the sinus into which they empty). This explains why the corresponding areas of the brain can be functionally and metabolically affected, but not irreversibly anatomically damaged [5, 51–53].

As local cerebral vein pressure continues to increase, with an exceeded collateral circulation, a progression of the clot within cerebral veins tributaries will significantly decrease the cerebral perfusion pressure. Consequently, the blood-brain barrier will be affected, producing vasogenic edema, cytotoxic edema producing local venous infarcts, and venous and capillary lesions with subsequent cerebral or subarachnoid hemorrhages [5, 51–53].

The decrease of the cerebral channels drainage secondary to their thrombosis produces an increase in venous and capillary pressure, with causing vasogenic edema,

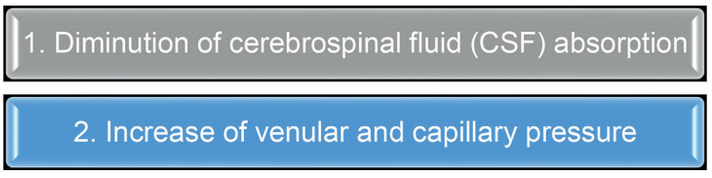

Figure 2.
Pathophysiology of cerebral veins and dural sinuses thrombosis.

with leakage of blood plasma into the interstitial space of the white matter/inside the glial cells, under the control of the hydrostatic pressure and osmotic gradients. This type of edema does not determine neuronal lesions, because the fluid in excess in the extracellular space can be evacuated [5, 51–53]. The increased intravenous pressure may lead to a decrease in cerebral perfusion pressure, resulting in diminished cerebral blood flow and consecutive failure of energy metabolism. This allows intracellular entry of ions and water across the cell membranes into neurons, from failure of the Na+/K+ ATPase pump and subsequent cytotoxic edema. In consequence, cytotoxic edema is an intracellular edema, caused by ischemia, producing the dead of neurons [5, 51–53].

Advances in understanding the pathophysiology of cerebral veins and dural sinuses occlusion have been obtained by the use of diffusion-weighted MRI and perfusion-weighted MRI, which have demonstrated the coexistence of both cytotoxic and vasogenic edema in patients with CVT [5, 51–53]. In cerebral venous infarcts, vasogenic edema is the majority in comparison with cytotoxic edema, thus explaining why cerebral venous infarcts differ from arterial ones and have a better prognosis [3, 51–53]. Brain edema and associated augmented intracranial pressure determine headache, vomiting, and diminished consciousness. In the situation of severe pressure differences, consecutive brain herniation can produce death [3].

The increase of the venous and capillary pressures determines cerebral vessel damage and erythrocyte diapedesis due to disruptions of the blood-brain barrier both resulting in cerebral hemorrhage. The neuronal lesions induced by the venous hemorrhages are usually minor than those produced by the arterial ischemic strokes [51–53].

Histological assessment in CVT patients identifies dilated brain veins, brain edema with compressed gyri, decreased sulci, small ventricles due to compression, and ischemic neuronal damages. The brain venous clot resembles different venous clot (an acute clot contains a majority of red blood cells—RBC—and fibrin and a minority of platelets; a chronic thrombus is substituted by fibrous tissue, usually with permeabilization) [3].

6. Clinical diagnosis

The clinical presentation and outcome of CVT are determined by multiple aspects, such as position and amount of occluded venous channels, the status of collateral pathways, the possible association of parenchymal lesions (cytotoxic or vasogenic edema, hemorrhage), age, gender, risk factors, and interval from clinical onset to treatment [4, 6]. Frequently, the clinical spectrum of CVT can be polymorphous, and misleading, usually with a subacute onset (in 50–80% of cases) [3, 54].

6.1 Clinical syndromes

In neonates, frequently CVT present a polymorphous clinical picture, with tetraparesis, seizures, and encephalopathy [19]. In older children, the clinical picture is similar to adults, especially with headache and paresis [55]. In elderly patients, encephalopathy is more frequent than in adults, whereas intracranial hypertension is unusual [1–4].

Usually, in adults with CVT, four clinical syndromes have been observed in combination or isolation: intracranial hypertension, focal neurological deficits, seizures,

and encephalopathy [1–4]. Only a minority of adult CVT cases present distinctive clinical syndromes, such as painful ophthalmoplegia (due to cavernous sinus thrombosis), or condylar jugular syndrome-with IX-XII cranial nerves palsies (due to IJVs, or posterior fossa vein thrombosis) [1–4].

6.1.1 Intracranial hypertension

It is the most frequent clinical syndrome detected in CVT patients (40% of cases) [8], being composed of headache, associated with vomiting, papilledema, visual complaints, and sixth nerve palsy [54]. This syndrome appears usually in cases with a chronic onset [56, 57].

Headache is the most frequent symptom detected in CVT cases (about 90% of patients in the ISCVT cohort). Usually, it may appear initially isolated, and it is more frequent in females and younger adults than in males or older patients [54, 55]. Headache from CVT is polymorphic: It may be localized or diffused [56]; usually, it is severe increasing during the night and can get worse with Valsalva maneuvers or position changes (when the patient is lying down) [2, 32]. Sometimes, it resembles a migraine with aura [58], and rarely, it appears like a thunderclap headache (mimicking a subarachnoid hemorrhage) [59]. Different risk factors for CVT (meningitis, epidural or brain abscesses, meningiomas, dural arteriovenous fistulas, vasculitis) develop headache. This symptom appears more frequently in CVT cases than in patients with cerebral arterial infarcts [3, 8].

Papilledema is noted on fundoscopy in 25–40% of CVT patients, especially in those with chronic onset. It can determine transient loss of vision (usually accompanied by severe headache), and, if prolonged, optic atrophy and subsequent peripheral blindness [8, 14].

6.1.2 Focal neurological deficits

According to different studies, they are observed in 37–50% of all CVT cases and are detected at onset in 15% of CVT patients [3, 9]. Paresis, usually paraparesis, is the most common sign (in the ISCVT cohort was observed in 37% of CVT patients) [3, 9]. Additional focal neurological deficits are more rare, such as Wernicke aphasia (appears in left transverse sinus occlusion connected with a posterior left temporal cerebral venous infarct), hypoesthesia, hemianopia, and ataxia (which is noted in posterior fossa veins thrombosis) [9]. Rarely, mixed transcortical aphasia is observed in left thalamus lesions due to deep cerebral vein thrombosis [60].

6.1.3 Seizures

They can appear as focal or generalized seizures, even status epilepticus, especially during the evolution of CVT (in the ICSVT cohort in 40% of patients) [9], and less often at the onset of CVT (12–15% of cases) [61, 62]. Seizures develop more frequently in patients with CVT who present motor deficits, and with supratentorial parenchymal brain lesions, which are the result of thrombosis of the SSS and tributary cortical veins [61, 62]. A higher incidence of seizures has been noted in peripartum (76%) [62] and neonates (44%) [63]. Seizures are more frequently in CVT than in arterial strokes [61–63].

6.1.4 Encephalopathy

Subacute/chronic encephalopathy is more frequent than acute encephalopathy. This syndrome consists of impaired mental status with cognitive impairment (such as delirium, apathy, and dysexecutive syndrome), and decreased level of consciousness (varying among stupor and profound coma). Commonly, it is related with different focal neurological deficits and it is usually detected in ageing or neonate cases [17, 64]. Sometimes, the decrease in the level of consciousness is reversible; nevertheless, coma at clinical onset is the key predictor of a poor outcome [1–4].

6.2 Topographic clinical diagnosis

Because of different factors, such as frequent simultaneous multiple cerebral veins and dural sinuses thrombosis (more than two-thirds of CVT patients), different anatomic variants and anomalies of cerebral venous channels, and the status of the venous collateral circulation, the topographic clinical diagnosis of CVT is not so well-defined like in arterial infarcts [3, 9, 65]. Nevertheless, isolated occlusion of cerebral venous channels determines the following clinical characteristics (**Figure 1**).

6.2.1 Superior sagittal sinus (SSS) thrombosis

It is the commonest dural sinuses thrombosis, particularly during the puerperium (62–80% in associated occlusion and 30% in isolated thrombosis, respectively) [3, 8, 14]. Usually, it appears as an isolated intracranial hypertension syndrome. The clinical spectrum may vary depending on the simultaneous thrombosis of other cerebral venous channels, especially of the bilateral tributaries' superficial cerebral veins. In this last situation, bilateral motor/sensory signs (especially in the legs) and psychiatric symptoms (prefrontal syndrome) may be detected due to bilateral frontoparietal hemispheric lesions [3, 8, 14].

6.2.2 Lateral sinus (LS) thrombosis

LS thrombosis may develop various clinical pictures. Usually, patients with isolated LS occlusion present intracranial hypertension (pseudotumor) syndrome; less often, they accuse isolated headache. Some patients may also develop associated focal neurological deficits due to cerebral lesions determined by the progression of the LS thrombosis to tributaries' cerebral veins. Thus, fluent Wernicke aphasia appears in left transverse sinus thrombosis associated with tributaries left temporal cortical vein thrombosis (40%), frequently in association with right hemianopia or superior quadrantanopia. Right temporal lobe lesions determine only left hemianopia, without aphasia. Nystagmus and gait ataxia characterize cerebellar lesions subsequent to LS thrombosis associated with tributaries posterior fossa veins thrombosis [3, 9, 65]. Due to the fact that the left LS is sometimes hypoplastic (10–14%), the intracranial hypertension syndrome occurs especially after right LS occlusion. In such situations, a bilateral venous drainage impairment may be detected concerning the basal regions of temporal lobes and cerebellum, with corresponding temporal lobe and cerebellar signs [1–4, 65].

The infectious etiology is much more frequent in LS thrombosis than in SSS occlusion. Thus, otitis, mastoiditis, or sinusitis can produce septic LS thrombosis: "otitic

hydrocephalus" [3, 65]. In this situation, the patient presents a relatively characteristic clinical picture with fever, headache, nausea and vomiting, vertigo, diplopia produced by sixth nerve palsy, neck pain, neck tenderness, and temporal and retro-orbital pain due to symptomatic trigeminal neuralgia [3, 65]. Sometimes, isolated LS thrombosis (clinically manifested with an isolated headache) could be produced by severe thrombophilia, without any associated infection (such as otitis) [5, 65, 66]. This is the reason why screening for LS thrombosis has to be performed in young females with isolated acute headache without otitis or mastoiditis [65, 66]. Rarely, LS thrombosis may produce isolated pulsating tinnitus [67].

6.2.3 Cavernous sinus thrombosis

It is rare and usually has an infection etiology, such as pyogenic infections of the face or of the paranasal sinuses [68, 69]. In cases with acute unilateral septic cavernous sinus thrombosis, they develop a peculiar clinical spectrum, with painful ophthalmoplegia, usually associated with proptosis, chemosis, conjunctival edema, papilledema, and retinas hemorrhages (due to ophthalmic superior vein thrombosis). If a fast diagnosis and an adequate treatment are missing, it progresses bilateral *via* intercavernous sinuses. When the clot extends to other venous channels, seizures and paresis may appear [68, 69]. In some situations, such as thrombophilia, surgery on intracranial or facial structures, and occlusion of dural arteriovenous fistulas, an aseptic cavernous sinus occlusion may be detected, with a poor clinical picture represented by an isolated abducens nerve palsy and mild proptosis [68].

6.2.4 Superior and inferior petrosal sinuses thrombosis

Usually, it is a sequela of cavernous or sigmoid thrombosis. The occlusion of the superior petrosal sinus clinically occurs as an isolated trigeminal palsy, while the thrombosis of the inferior one appears as an isolated abducens palsy [1–4].

6.2.5 Cortical vein thrombosis

Isolated occlusion of superficial cerebral veins is rarely detected (only 2% of all CVT cases), but it is certainly underdiagnosed, due to difficulties to identify this disease using traditional MRI sequences (spin-echo) and MR venography [70]. Occlusion is detected especially at the level of the superior superficial cerebral veins, with a clinical spectrum consisting of seizures associated with focal neurological deficits, such as motor/sensory deficits or aphasia [70].

6.2.6 Deep cerebral vein thrombosis

This type of cerebral vein thrombosis is usually associated with the occlusion of the SS; it rarely appears, more often in neonates. In such cases, its clinical picture is severe, with encephalopathy, and tetraparesis [71, 72]. In adults, a more limited occlusion of the deep cerebral veins, without associated SS thrombosis, can determine milder clinical features, especially headache, vomiting, gait ataxia, alternating hemiparesis or tetraparesis, neuropsychological symptoms, and even minor troubles of consciousness [71, 72]. Exceptional, "benign" cases of occlusion of the deep cerebral veins were reported with only mixed transcortical aphasia [60].

6.2.7 Posterior Fossa vein thrombosis

Isolated posterior fossa vein occlusion rarely occurs, because these veins possess efficient collateral pathways. However, it is the main differential diagnosis in patients with different risk factors for CVT, which present some clinical aspects (intracranial hypertension syndrome, and cerebellar-vestibular syndrome), and atypical features on brain CT, such as bilateral cerebellar infarcts or irregular cerebellar hemorrhages [73, 74].

6.2.8 Internal jugular vein (IJV) thrombosis

Usually, the IJV thrombosis appears as a progression of the sigmoid sinus thrombosis or may be determined by cannulation for long-term IJV access or can be subsequent of tonsillopharyngitis (Lemierre's syndrome). IJV occlusion can be asymptomatic, or it can manifest itself in the form of a local infection (pain and tender of the mastoid, and a painful and swelling occluded IJV). A jugular foramen syndrome (consisting of unilateral pulsatile tinnitus [67] or multiple low cranial nerve palsies VIII-XII) develops if the infection disturbs the skull base [75].

6.2.9 Emissary vein (EV) thrombosis

The emissary veins (e.g., petrosquamosal sinus (PSS)) are vestigial veins, which present no valves and link the dural sinuses with the extracranial veins. Posterior fossa EVs cross through different cranial orifices and guarantee (with the IJV) a supplementary extracranial venous empty of the posterior fossa veins. On one hand, in healthy subjects, EVs are small and asymptomatic. On the other hand, in pathological situations (such as high-flow arteriovenous malformations, IJV aplasia, or IJV, or LS occlusion) EVs become large with clinical significance (different craniofacial syndromes and pulsatile tinnitus) [67, 74].

7. Laboratory tests

Unfortunately, apart from neuroimaging, there is no simple confirmatory laboratory test that can surely exclude acute CVT.

7.1 Blood assay

According to Guidelines from the American Heart Association/American Stroke Association (AHA/ASA) a comprehensive blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time are mandatory for patients with clinical suspicion of CVT [14]. The results from these tests may detect pathological processes that produce CVT, such as a hypercoagulable state, infective, or inflammatory diseases. Antiplatelet factor four (PF4) antibodies are examined for COVID 19-vaccination-associated CVT [47]. On one hand, the screening for use of OC is suggested at the first assessment of young females with clinically suspected CVT, and, on the other hand, the screening for an occult neoplasm is indicated in CVT cases older than 40 years [14, 76].

7.2 D-dimer

A high plasma D-dimer level recommends the diagnosis of CVT, but a normal plasma D dimer level does not eliminate the CVT diagnosis, especially in those situations with associated risk factors and a clinical picture compatible with CVT, such as isolated headache in young females [77, 78].

7.3 Lumbar puncture and cerebrospinal fluid (CSF) assessment

Both techniques may be suitable to eliminate meningitis in those CVT patients with isolated intracranial hypertension syndrome, and in cases with sepsis, or with fever and no clear source of infection [9, 79]. An augmented opening pressure during the assessment of CSF pressure is usually detected in CVT patients with isolated intracranial hypertension. Nevertheless, CSF assessment is not useful for cases presenting focal neurologic deficits and neuroimaging data suggestive for CVT. Unfortunately, the CSF anomalies in CVT are generic, such as lymphocytosis, hyperproteinorahia, and abundant red blood cell count, and are detected between 30 and 50% of all CVT patients [79]. Lumbar puncture is contraindicated in CVT cases with large parenchymal lesions, due to a high risk of herniation [8, 79].

7.4 Evaluation for thrombophilic state

Investigating for thrombophilia should be done for those patients who have an important possibility of severe thrombophilia (such as an individual and/or family history of systemic or cerebral venous occlusion, CVT in young adults, or in cases without a risk factor for CVT) [6]. When specified, screening should comprise factor V Leiden, prothrombin G20210A pathologic variant, homocysteine, antithrombin, protein C, protein S, lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein-I antibodies [9, 76].

8. Neuroimaging

Neuroimaging techniques are mandatory for the diagnosis of CVT [76, 80].

8.1 Head computed tomography (CT)

Head CT is generally the initial method to be done in the emergency department in patients with acute clinical doubt for CVT [12]. It should be realized primarily without contrast enhancement (NCECT), and subsequently (if intracranial hemorrhage is not detected) with contrast enhancement (CECT) (**Table 1**) [1, 14, 76, 80].

The main advantages of head CT are: a) it may diagnose other diseases that CVT can clinically be like, such as subdural hematoma, abscess, or neoplasms; b). it may detect diseases that can themselves determine CVT, such as sinusitis, mastoiditis, abscesses, or meningiomas; c). it can identify direct and indirect signs of CVT [3, 76, 80].

8.1.1 Direct signs of CVT on head CT

They signify the direct imagining of the venous thrombus inside the occluded cerebral venous channel and can be detected in 30% of all CVT cases. They are

Direct signs	Indirect signs
• Dense triangle sign (acute clot in dural sinus on NCECT) • Replacement of normal dark flow void with a clot on MRI • Cord sign (acute thrombosed cerebral vein on NCECT) • MRI equivalent: acute thrombosed cerebral vein on T2* GRE images or T2*SW images. • Empty delta sign (chronic clot in dural sinus) on CTV/ contrast enhancement-MRV	• Cerebral edema (on CT or MRI-T1 WI/ T2WI) with elevated or mixed diffusion characteristics (on DWI) • Hemorrhagic infarction • Subarachnoid hemorrhage • Subdural hemorrhage

Table 1.
Computed tomography (CT) and magnetic resonance imaging (MRI) features in CVT [1].

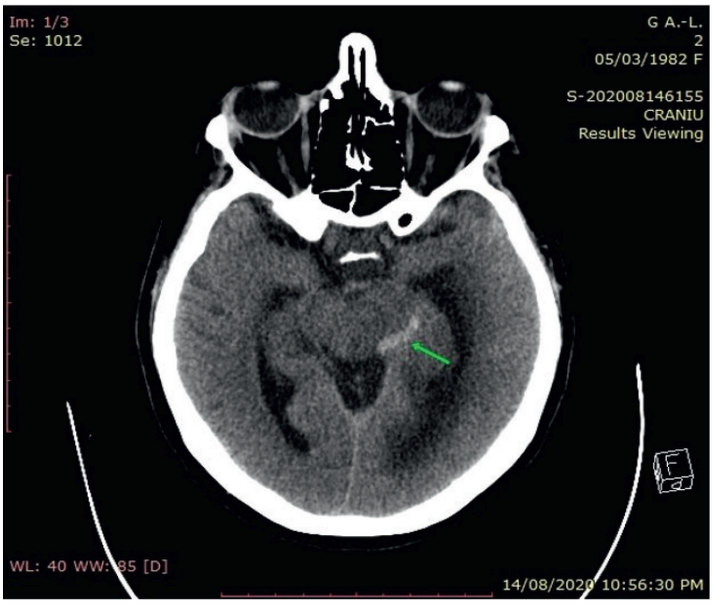

Figure 3.
Non-contrast head CT performed in the acute phase shows hyperdense appearance (acute thrombosis) of the left latero-mesencephalic vein [60].

represented by the "cord sign," the "dense triangle sign," and the "empty delta sign" [8, 76, 81, 82].

The "cord sign" characterizes an acute occluded cerebral vein on NCECT and is detected in 25% of all CVT patients. It looks as a curvilinear or linear hyperdensity determined by a fresh clot in-side a thrombosed cerebral vein (**Figure 3**) [60]. It can be detected during the first week of the disease [10]. After this period, the clot becomes isodense and then hypodense. Mimicking is detected in slow-flow patients; consequently, its specificity is considered to be rather low [3, 76, 80].

The "dense triangle sign" represents a fresh clot inside a dural sinus on NCECT, detected in only 1–2% of all CVT cases [80]. It looks as a triangular or round hyperdensity inside the sinus (usually the posterior part of the SSS) [8]. It is best imagined during the first 2 weeks from CVT clinical onset. As cases with increased hematocrit or dehydration can also determine this sign, and its specificity is low, particularly in other sinuses than SSS [81–83]. Venous sinus density quantification and Hounsfield unit-to-hematocrit (H:H) ratio have been observed to increase the sensitivity in diagnosing CVT, as attenuation of 62HU and higher is indicative of thrombosis [84].

The "empty delta sign" is observed on CECT scans in 10–20% of all CVT patients, between days 5 and 2 months after onset. It looks as a triangular hyperdensity of contrast enhancement of the walls of the sinus surrounding a hypodense central area without contrast enhancement inside the dural sinus (usually the posterior part of the SSS) [85, 86]. The sensitivity and specificity of this sign are increased to 30% of all CVT patients with CT exams with orthogonal sectioning, different window and level settings, and multi-planar reformations. Additionally, an premature separation of the SSS can be confused with this imagistic feature; consequently, it is not pathognomonic specifically characteristic for CVT [85, 86].

8.1.2 Indirect signs of CVT on head CT

These signs are more common than direct signs and are the following [9, 14]:

The intense contrast enhancement of falx and tentorium denotes stasis or hyperemia of the dura mater and appears in 1/5 of all CVT patients. The former is usually problematic to detect in chronic cases, but the latter is observed without difficulty, specifically representing SS and SSS occlusion [1–4, 85].

The cerebral veins may look dilated on the native CT assessment, due to their anatomic peculiarities (they possess thin walls, without a muscular tunic) [85]. Diffuse brain edema (20–50% of all patients) can subsequently determine an effacement of cerebral sulci and small ventricles; this latter feature may be hard to discriminate from typical aspects with small ventricles in young patients [9, 85]. The detection of the reverse sign (enlarged ventricles) cannot eliminate the CVT diagnosis, as it may be determined by the hydrocephalus due to increased CSF creation and decreased reabsorption due to increased cerebral venous pressure. Frequently, it is the hallmark of posterior fossa veins thrombosis. In both situations (small vs. enlarged ventricles), a judgment with anterior CT exams is mandatory [9, 85].

Cerebral parenchymal abnormalities may be divided into nonhemorrhagic and hemorrhagic and may be identified in 60–80% of all CVT patients [85]. The former type of abnormalities comprises extensive areas of hypodensity, produced by diffuse brain edema, as well as focal zones of hypodensity formed by loco-regional edema or cerebral venous infarction, not respecting the arterial borders. With serial imaging, some of these abnormalities may disappear ("vanishing infarcts"), and new parenchymal anomalies may be observed. The latter type of parenchyma abnormalities contains hemorrhagic infarcts, intracerebral hemorrhage, or rarely subarachnoid hemorrhage (**Figure 4**) [8, 60, 85].

Some types of CVT may develop on CT peculiar aspects.

First, numerous irregular filling defects with distended cavernous sinuses and orbital veins on CECT are mandatory for cavernous sinus thrombosis [14, 76]. Second, bilateral parasagittal hemispheric lesions are very evocative for occlusion of the SSS. [14, 76] Third, temporo-occipital lesions designate LS or vein of Labbe thrombosis [14, 76]. Fourth, in patients with acute deep cerebral veins occlusion, they present bilateral hypodensities, representing thalami, basal ganglia, and internal capsule infarcts; bilateral hyper-densities with the same location, determined by acute cerebral hemorrhages or hemorrhagic infarcts; extensive edema with compression of the third ventricle and subsequent hydrocephalus, and a hyperdense area inside the occluded sinuses, due to a fresh clot. In consequence, the presence of hemorrhage or edema adjacent to a cerebral venous channel should recommend CVT [14, 76]. Fifth, cerebellar venous infarctions can produce hydrocephalus and compression of the fourth ventricle [14, 76].

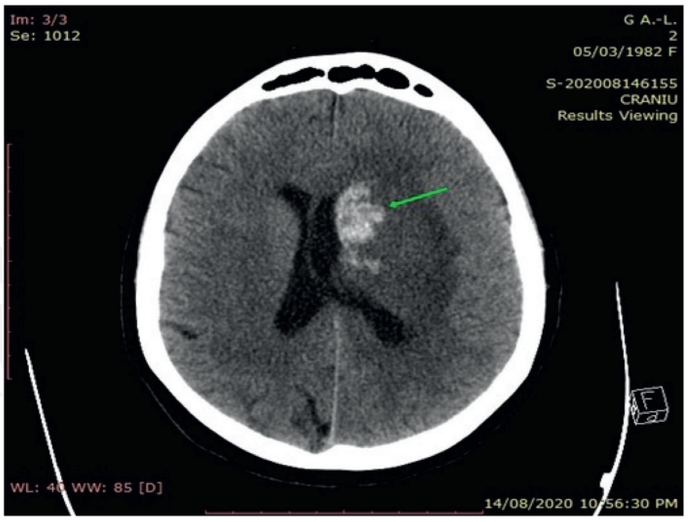

Figure 4.
Non-contrast head CT performed in the acute phase shows venous infarction with hemorrhagic transformation in corpus of the left caudate nucleus [60].

Regrettably, head CT detection of CVT is insensitive, results being pathological only in 30% of true CVT subjects, and all CT signs are nonspecific in the other patients [14]. Additionally, different anatomic variants may mimic sinus occlusion, such as sinus atresia or hypoplasia, asymmetric sinus drainage, and normal sinus filling defects related to arachnoid granulations or intrasinus septa [14, 76]. Consequently, a normal Head CT will not eliminate a CVT. So, in clinically supposed cases, a CT venography or MRI venography is mandatory for CVT detection [81, 82].

8.2 CT venography-CTV (multi-detector CT angiography-MDCTA) with bolus injection of contrast material

Usually, CT venography (CTV) is done especially in acute CVT patients, immediately after NCECT. It certifies an excellent detection of the venous channels (high-density contrast in patent segments) (**Table 2**) [1].

CTV can distinguish both direct signs of thrombosis (filling defects, with low density in the occluded venous channels) and indirect signs (sinus wall enhancement and increased collateral venous circulation). Supplementary, in subacute or chronic CVT cases, CTV can detect a heterogeneous thrombus (**Table 2**) [8, 85].

When CTV accompanies head CT, their combined accuracy is 90–100%, depending on the obstruction location [86–90].

CTV presents some advantages versus digital subtraction intra-arterial angiography (DSA): It is cheaper, less invasive, and quicker (due to a faster image acquisition). CTV identifies better the ISS, the cavernous sinuses, and the basal vein of Rosenthal (with multiplanar reformatted images) than DSA [87–90]. Compared with DSA, the combination of CT/CTV has a sensitivity and specificity of 95 and 91%, respectively [14].

CTV offers some advantages compared to magnetic resonance venography (MRV): It is much more reachable, cheaper, faster, has no contraindications to ferromagnetic devices, amplified imaging resolution for the main dural sinuses, easier to comprehend, and has fewer artifacts than MRV. CTV presents a similar accuracy as time-of-flight (TOF) MRV in the detection of the dural sinuses, with

Imaging method	Advantages	Disadvantages
CTV	• More widely accessible than MRV • Generally, costs less than MRV • Faster image acquisition than MRV • More suitable for unstable patients. • Less prone to motion artifact. • Better detection of cerebral small vessels.	• Radiation risk • Higher rate of adverse reactions to iodinated contrasts, including the risk of contrast-induced nephropathy. • Potentially reduced visualization of skull base structures in 3D display. • Acute thrombus, which is hyperdense, may mimic opacified sinus, resulting in false-negative results.
MRV	• No radiation risk • Low rate of adverse reactions to Gadolinium. • Indicated in cases with severe renal failure if done without contrast enhancement contrast technique). • Higher sensitivity for small parenchymal lesions.	• Contraindicated in cases with ferromagnetic devices and most pacemakers. • More prone to motion artifact. • TOF-MRV may present false-positive results from a flow that has a parallel direction with the acquisition plane. • For this reason, phase-contrast MRV has to be used to identify the thrombus. • Stenotic, hypoplastic, or aplastic dural sinuses may be misdiagnosed as CVT.
CTV and MRV	Noninvasive imaging methods with indirect signs possible to detect.	• Inferior resolution to detect the patency of the posterior part or entire SSS, both LSs of the deep cerebral veins to DSA.

Table 2.
Comparison of CTV and MRV in CVT [1].

higher ability versus MRV to detect: the ISS and the nondominant transverse sinus occlusion; the single cortical vein thrombosis; and venous channels with low flow [87–90]. Regrettably, CTV is less sensitive in the valuation of the superficial and deep cerebral veins than in that of the dural sinuses. This weakness can be perfected by using multiplanar reformations, which growths the sensitivity of CTV beyond DSA [87, 88]. Unfortunately, maximum intensity projection (MIP) image generation has reduced recognition of skull base components in three-dimensional display, with unintended sinus omission from bone subtracting algorithms. Nevertheless, this can be ameliorated with specific software for mask bone elimination [90]. CTV also has some disadvantages, such as contrast allergy, contrast nephropathy due to contrast material, and radiation exposure, which may contraindicate its usage during pregnancy or renal failure [90].

8.3 Magnetic resonance imaging (MRI) of the head

Unenhanced MRI is a more sensitive technique for detecting CVT than NECT. Patent dural sinuses can be seen as flow voids (hyposignal on T1, and T2 WI) on MRI [91, 92].

MRI pathological signs in CVT patients consist of direct signs (detecting the thrombus itself inside the venous channel) and indirect signs, respectively (lesions secondary to venous occlusion, perceived especially at the level of the cerebral parenchyma) [91, 92].

8.3.1 The MRI direct signs

The key signs of thrombosis are represented by the replacement of normal dark flow void (which certifies the presence of flow inside a patent venous channel) with the absence of a flow void (which denotes the absence of flow in an occluded cerebral venous channel). The signal intensity of the venous clot on T1- and T2-weighted MR images is comparable to a hematoma, and it is developing dependent on thrombus oldness. The consecutive signal intensity changes observed in the thrombus are the consequences of the paramagnetic aspects of the hemoglobin and its degradation products (i.e., hemosiderin, methemoglobin, deoxyhemoglobin) (**Table 3**) [82, 91–96].

a. In the acute phase (the first 5 days after the clinical onset), the flow void is missing (the vessel is occluded with absence of flow) and the thrombosed venous channel is isointense with brain tissue on T1-WI and hypo/isointense on T2-WI, as a result of the richness of deoxyhemoglobin in RBC inside the thrombus. The recognition of CVT (fresh venous clot) in the acute stage is problematic on single conventional MRI, because the MRI signs are comparable to normal venous flow. Therefore, other MRI sequences, MRV, CTV, or DSA are required to identify the absence of flow in the occluded cerebral veins or dural sinuses [91, 92].

b. In the subacute phase (between 6 and 15–30 days after the clinical onset), the thrombus becomes more apparent because the signal is hyperintense in both T1- and T2-WI, due to the accumulation of methemoglobin inside the clot. These imaging signs are specific for CVT and are the most common imagistic features (**Figure 5**) [89–92].

c. In the chronic stage (between 2 and 4 weeks after the clinical onset), the commencement of recanalization of the previously thrombosed venous channel produces the reappearance of the flow void (the vessel is now patent). In this stage, the venous thrombus, which is heterogeneous, is isointense on T1-WI, with variable intensity (iso/hyperintense) on T2-WI, due to the deoxygenated hemoglobin and methemoglobin components. Therefore, in this stage, the diagnosis of CVT can be unnoticed [91, 92].

After 4–6 months, no signal anomaly is observed on T1-WI or DWI; nevertheless, delicate changes (heterogeneous topic signal abnormalities) can be detected in T2-WI or FLAIR, which can persist for years, and should not be interpreted for a recurrent acute CVT [91, 92].

	Normal sinus	**Thrombus less than 5 days old**	**Thrombus from D5 to D30**	**Thrombus older than 1 month**
T1	Hyposignal	Isosignal	Hypersignal	Iso/hypersignal
T2	Hyposignal	Hypo/isosignal	Iso/hypersignal	Iso/hypersignal
Contrast-enhanced T1	Homogeneous because the fresh thrombus can be enhanced	Empty delta sign	Empty delta sign	Empty delta

Table 3.
The evolution of the thrombus signal [82].

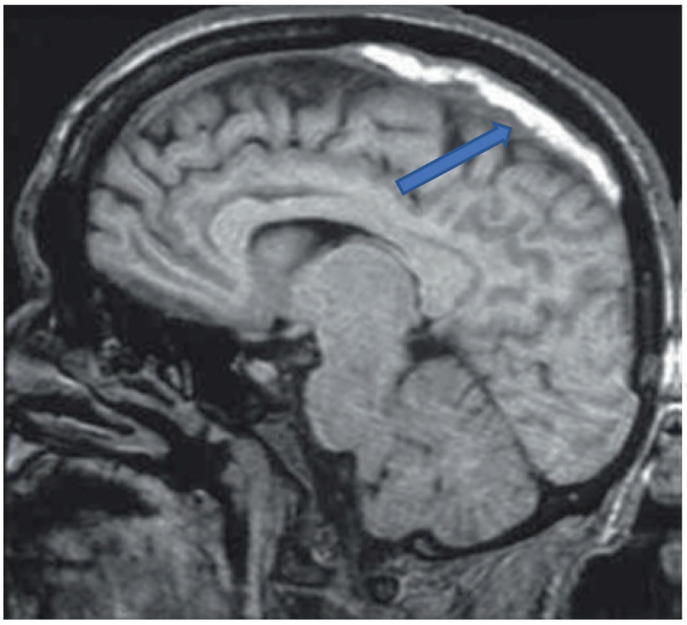

Figure 5.
MRI midline sagittal T1-weighted image. Blue arrow—hyper-intense signal indicating subacute thrombosis of the SSS; this pattern was found 14 days after the onset of symptoms.

Regrettably, in a substantial percent of cases, we can notice false-negative or false-positive appearances. The false-negative situations are infrequent and characterize a supra-acute or chronic stage, or a single superficial cerebral vein occlusion, which will be detected mainly by DSA. The false-positive conditions are the consequence of slowly cerebral venous flow. To diminish both artifacts, we have to change the position of the subject, to repeat the sequence in another plane, with two or more sequences, and with other types of sequences, as follows [76, 85]:

Gradient echo T2-weighted (T2*GRE) MRI sequences*: Recognize CVT, as degradation products, which can determine augmented signal drop-out, identifying intravenous channels thrombus in stages where the clot can be barely visible in other sequences [93]. Consequently, on T2*GRE MRI sequences, the fresh thrombus can be identified as an area of hypointensity in the affected venous channel. Nevertheless, a chronically occluded dural sinus may still present hypo signal on *T2*GRE* [94].

*Echo-planar T2 susceptibility weighted imaging (T2*SWI) MRI sequences*: It is a complementary T2* GRE sequence to assess CVT. SWI detects the acute isolated superficial cerebral veins occlusion, when both T1 and T2 are less sensitive. It identifies the intraluminal thrombus as a hypointense area. The exaggeration of magnetic susceptibility effect (MSE) aids recognition of discrete thrombosis, and supplementary, this sequence distinguishes cerebral venous stasis, existence of collateral circulation, and intracranial hemorrhage [95]. Complementary, SWI shows a blooming artifact better detected than T2* GRE, determining a better position of the clot or hemorrhage. Isolated superficial cerebral vein occlusion may be easier to diagnose on the maximum-intensity projections (MIPs) of SWI compared to dedicate venous imaging [82, 95].

8.3.2 The MRI indirect signs

Different cerebral lesions secondary to venous channel occlusion, such as brain edema, cerebral infarct, and/or cerebral hemorrhage, observed in CVT patients are better identified by MRI than by CT [81].

Cerebral edema and cerebral venous infarction determine both a hypersignal on T2-WI and an isointense/hypointense signal on T1-WI. Isolated cerebral edema, without associated cerebral venous infarcts or cerebral hemorrhages, may be detected in near half of CVT cases and may be accompanied with cortical sulcal effacement and small ventricles. When these MRI features are identified, CTV or MRV should be done to endorse the CVT diagnosis [91, 92].

Cerebral hemorrhage is characterized by a hypersignal in both T1- and T2- WI, occurring in 30% of all CVT cases. Frequently, SSS thrombosis may be associated with flame-shaped, irregular, and heterogeneous bilateral parasagittal areas of frontoparietal hemorrhages. Usually, LS occlusion is accompanied by both temporal and occipital lobes lesions. The occlusion of the vein of Galen or of the SS may be associated with bilateral deep brain lesions, such as thalamic hemorrhages, intraventricular hemorrhages, or wide brain edema [91, 92].

Unfortunately, there is no simple confirmatory MRI indirect sign for CVT, but their significance is clear because of the concomitant MRI direct signs for CVT [91, 92].

Diffusion-weighted imaging (DWI) techniques: DWI detects the thrombus as a hypersignal inside the occluded venous channel, with a reduced apparent diffusion coefficient (ADC). Patients with restriction on DWI have extended recovery time and lower probability of total clot recanalization (DWI-prognostic factor) [14, 96] (**Figure 6**).

DWI identifies cerebral edema, which may be divided in:

- Vasogenic edema, presenting diverse signal deviations in the damaged regions, and raised ADC values, lacking lesser ADC values than in health areas [1, 94].

- Cytotoxic edema, presenting a hypersignal, and low ADC values [1, 94].

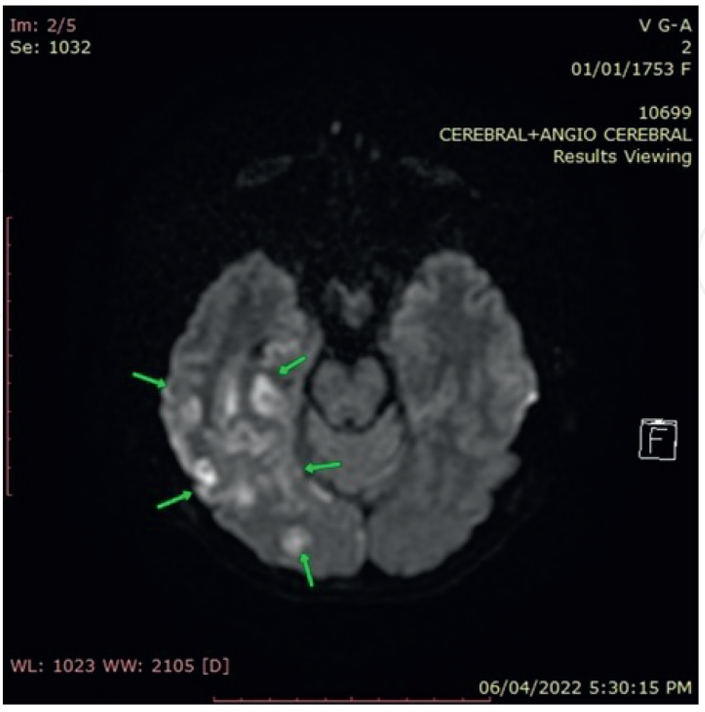

Figure 6.
DWI-b1000. Non-contrast head MRI performed in the acute phase shows a large venous infarction in right temporal lobe (arrows).

On perfusion-weighted (PWI) MRI, relative cerebral blood volume (rCBV), and mean transit time (MTT) are augmented in damaged regions, with conserved relative cerebral blood flow (rCBF) [1–4, 96].

Usually, in CVT patients, the vasogenic edema is prominent versus cytotoxic edema; in consequence, the corresponding cerebral areas may be functionally and metabolically affected, but not irreversibly. The reversibility of venous brain lesions is emblematic for CVT patients, determining both a better recovery in venous cerebral ischemic strokes than in arterial infarcts and vanishing lesions on MRI, respectively [91–96].

8.4 Magnetic resonance venography (MRV)

MRV may be realized without contrast enhancement (using TOF technique or phase-contrast technique) or with a contrast-enhanced technique [97, 98].

8.4.1 The two-dimensional (2D-TOF) technique (with 1.5- and 3-mm thick slices in the coronal and axial planes)

This technique is mandatory in pregnant or breastfeeding females, or in patients with severe renal failure, where contrast enhancement is proscribed. It detects: a). the direct sign of CVT, represented by the absence of flow signal (nonappearance of opacification) of venous channel, though interpretation can be confused by different anatomic variants, like sinus hypoplasia, or asymmetric flow [97, 98]. b). The indirect signs of CVT comprise delayed emptying, collateral venous circulation, dilated veins, and tortuous collateral cortical veins (corkscrew veins) (**Figure 7**) [4].

2D-TOF technique is superior to its 3D counterpart, because it has a relative absence of saturation effects and superior sensitivity in the setting of slow venous flow but presents a low sensitivity to small cerebral veins with slow flow. One significant pitfall is that same-plane acquisition can produce false-positive results from saturation and subsequent signal nulling, as this technique is most sensitive to orthogonal flow [97, 98].

8.4.2 Contrast-enhanced (CE)-MRV (MRV with gadolinium)

MRV with gadolinium realizes a direct examination of luminal filling similar to that of CTV, with similar sensitivity and specificity (**Figure 8**). Both CTV and CE-MRV are superior to the TOF and phase-contrast (PC) techniques, due to different artifacts that may be observed in these sequences [85]. Regrettably, conventional MRV has some limitations: It has a diminished capacity in identifying cavernous sinus and superficial cerebral veins thrombosis, partial thrombosis of other dural sinuses and cerebral veins, or net distinction between hypoplasia and occluded sinus [8].

Different MR techniques may be suitable to distinguish between sinus hypoplasia and dural sinus thrombosis. T2*GRE or T2*SWI MRI sequences will distinguish a normal signal in a hypoplastic sinus and an abnormally low signal in the occurrence of a thrombus [93–95]. Supplementary, a chronically thrombosed hypoplastic dural sinus will have absence of flow on 2D-TOF MRV and enhancement on CE-MRI and MRV [8].

CE-MRV sequences should be differentiated from different anatomical 3D T1 sequences, such as SPGR, BRAVO, TFE, and FFE [2].

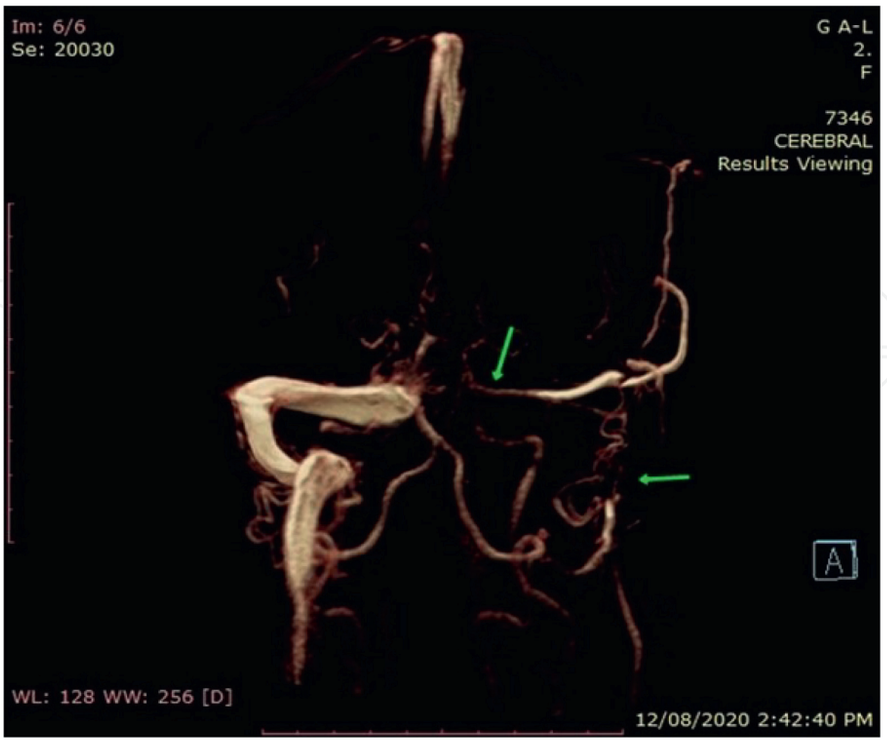

Figure 7.
3D-CORONAL VRT (reformatted by 2D-TOF venography) sequence shows an absent flow in left jugular bulb, left sigmoid sinus, left transverse sinus, and sinus confluence.

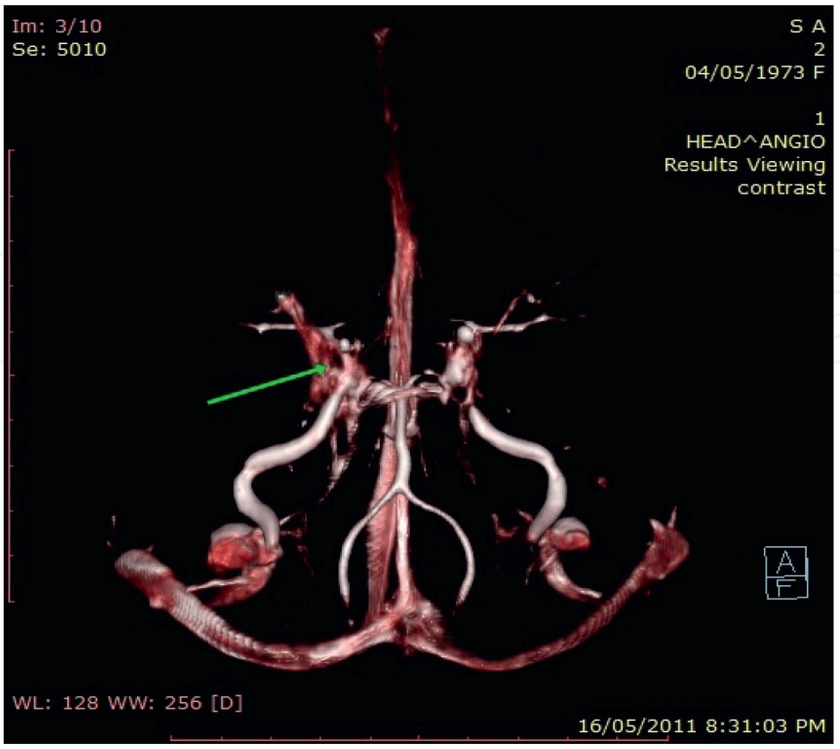

Figure 8.
3D-CORONAL VRT (reformatted by CE-MRA) sequence filling defect throughout the dural right cavernous sinus (arrow).

3D elliptical T1 post-gadolinium enhancement: It is a relatively newer technique, in which the paramagnetic effect of gadolinium shorts T1 and produces positive intravascular contrast enhancement [85, 98]. It realizes an improved assessment of the superficial and deep cerebral veins, and of the sinuses of the base of the skull (petrous, cavernous, and basilar plexus); an excellent detection of the lateral sinuses, even with hypoplasia; it overcomes the limitations of other MR techniques, especially signal losses in the situation of slow or turbulent flows (2D TOF, 2D, and 3D phase-contrast), not perpendicular to the acquisition plane (TOF) and in the event of unsuitable choice of encoding speed (2D and 3D phase-contrast) [85, 98].

3D phase-contrast (PC) MRV: It has a better capacity to detect slow flow and may better distinguish between slow flow and clot [97, 98]. Static contrast-enhanced 3D MRV detects better the cerebral veins and dural sinuses; unfortunately, it may present some restrictions in chronic dural sinus thrombosis as the clot may be enhanced, simulating a patent sinus [97, 98].

Time-resolved 3D MRV (4D MRV): This aspect is resolved with 4D MRV, which obtains images with diverse delays for better recognition of the venous clot [97]. This technique has better sensitivity to detect CVT than T2-WI, T2*GRE, and TOF-MRV; additionally, it has better specificity than TOF-MRV, and it recognizes better chronic CVT [97].

8.5 Cerebral intra-arterial angiography with venous phase imaging and direct cerebral venography

8.5.1 Cerebral intra-arterial angiography with venous phase imaging

It needs a four-vessel angiography (conventional or DSA) with detection of the whole venous phase on at least two projections (frontal and lateral) and three oblique views for the recognition on the entire SSS [14, 99].

Distinctive signs of CVT are represented by the following: partial deficiency of opacification or absence of filling of venous channels, late emptying, dilatation of cortical, scalp, or facial veins, dilatation of collateral veins, reverse of venous flow, and the abrupt ending of cortical veins encircled by tortuous and dilated collateral "corkscrew" veins [14, 99]. The obstruction of the posterior portion or the SSS, both LSs or the deep cerebral veins, is relatively easy to detect, but it can be misdiagnosed with hypoplasia or aplasia when the anterior third of the SSS or of the left LS is occluded [3, 14, 99]. Thus, we have to identify other imagistic features, such as occlusion of other cerebral vein or dural sinuses or delayed draining and dilatation of collateral veins in the occlusion of the anterior part of the SSS, or total absence of opacification of the whole sinus or its sigmoid segment in LS thrombosis, respectively [3]. This method presents some limitations: It does not detect the thrombus itself, and it is invasive, presents radiation exposure, possible allergy to the iodine contrast material, and requests teams of experts [3, 14, 99].

8.5.2 Direct cerebral venography

This technique is realized throughout endovascular therapeutic techniques, identifying the thrombus inside the venous channel either as an intra-vessel filling defect (no occlusive thrombosis) or as a complete no filling (occlusive thrombosis); complete obstruction by the clot may occur as a "cupping appearance" inside the dural sinus [14, 99]. Although the interobserver agreement for the detection of CVT is

not excellent, the association of angiography with MRI will increase the interobserver agreement than angiography alone (94% versus 62%) [99].

9. Conclusions

CVT adult patients are younger, predominantly females, and have diminished frequencies of classical vascular risk factors when compared with cases with arterial infarcts.

The main risk factors for CVT in adults are prothrombotic conditions, either genetic or acquired.

The pathophysiology of CVT regulates the clinical picture and the abnormal imaging features. The nonspecific clinical spectrum of CVT may produce delays in diagnosis and consists of headache or intracranial hypertension, seizures, focal neurological deficits, and/or encephalopathy.

Both CT-CTV and MRI-MRV are outstanding methods to diagnose CVT and to distinguish consecutive complications. They may be associated with better evaluation.

Author details

Dragos Catalin Jianu[1,2,3*], Silviana Nina Jianu[4], Nicoleta Iacob[5], Traian Flavius Dan[1,2,3], Georgiana Munteanu[1,2,3], Anca Elena Gogu[1,2,3] and Ligia Petrica[6]

1 First Division of Neurology, Department of Neurosciences-VIII, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

2 Centre for Cognitive Research in Neuropsychiatric Pathology (NeuroPsy-Cog), Department of Neurosciences, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

3 First Department of Neurology, "Pius Branzeu" Clinical Emergency County Hospital, Timisoara, Romania

4 Department of Ophthalmology, "Dr. Victor Popescu" Military Emergency Hospital, Timisoara, Romania

5 Department of Multidetector Computed Tomography and Magnetic Resonance Imaging, Neuromed Diagnostic Imaging Centre, Timisoara, Romania

6 Division of Nephrology, Department of Internal Medicine II, "Victor Babes", University of Medicine and Pharmacy, Timisoara, Romania

*Address all correspondence to: dcjianu@yahoo.com

IntechOpen

References

[1] Jianu DC, Jianu SN, Dan TF, Munteanu G, Copil A, Birdac CD, et al. An integrated approach on the diagnosis of cerebral veins and Dural sinuses thrombosis (a narrative review). Life. 2022;**12**:717. DOI: 10.3390/life12050717

[2] Sadik JC, Jianu DC, Sadik R, Purcell Y, Novaes N, Saragoussi E, et al. Imaging of cerebral venous thrombosis. Life. 2022;**12**:1215. DOI: 10.3390/life12081215

[3] Mohr JP, Choi DW, Grotta JC, Weir B, Wolf PA. Stroke (Pathophysiology, Diagnosis, and Management). 4th ed. Philadelphia, Pennsylvania, USA: Churchill Livingstone; Chapter 12; 2004. pp. 301-325. DOI: 10.1016/B0-443-06600-0/X5001-9

[4] Stam J. Thrombosis of the cerebral veins and sinuses. The New England Journal of Medicine. 2005;**352**(17):1791-1798. PMID: 15858188. DOI: 10.1056/nejmra042354

[5] Piazza G. Cerebral venous thrombosis. Circulation. 2012;**125**:1704-1709. DOI: 10.1161/circulationaha.111.067835

[6] Dmytriw AA, Song JSA, Yu E, Poon CS. Cerebral venous thrombosis: State of the art diagnosis and management. Neuroradiology. 2018;**60**(7):669-685. DOI: 10.1007/s00234-018-2032-2

[7] Grotta JC, Albers GW, Broderick JP, Kasner SE, Lo EH, Mendelow AD, et al. Chapter 45: Cerebral venous thrombosis. In: Grotta JC, Albers GW, Broderick JP, Kasner SE, EH LO, Mendelow AD, Sacco RL, LKS W, editors. Stroke. 6th ed. Vol. 45. Newcastle, United Kingdom: Elsevier; 2016, 2016. pp. 716-730. DOI: 10.1016/B978-0-323-29544-4.00085-2

[8] Ferro JM, Canhão P. Cerebral venous thrombosis: Etiology, clinical features, and diagnosis. Newcastle, United Kingdom: UptoDate; 2023

[9] Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: Results of the international study on cerebral vein and Dural sinus thrombosis (ISCVT). Stroke. 2004;**35**:664-670. DOI: 10.1161/01.str.0000117571.76197.26

[10] Caplan LR, Biller J, Leary MC, Lo EH, Thomas AJ, Yenari M, et al. Chapter 5: Anatomy of cerebral veins and Dural sinuses. In: Primer on Cerebrovascular Diseases. 2nd ed. Vol. 5. Cambridge, Massachusetts, USA: Academic Press; 2017. pp. 32-36. DOI: 10.1016/B978-0-12-803058-5.00005-9

[11] Satyarthee GD, Moscote-Salazar LR, Agrawal A. Persistent enlarged occipital sinus with absent unilateral transverse sinus. Journal of Neurosciences in Rural Practice. 2019;**10**:519-521. DOI: 10.1055/s-0039-1696081

[12] Valdueza JM, von Münster T, Hoffman O, Schreiber S, Einhäupl KM. Postural dependency of the cerebral venous outflow. The Lancet. 2000;**355**:200-201. DOI: 10.1016/s0140-6736(99)04804-7

[13] Coutinho JM, Zurbier SM, Aramideh M, Stam J. The incidence of cerebral venous thrombosis a cross-sectional study. Philadelphia, Pennsylvania, USA: Stroke. 2012;**43**:3375-3377. DOI: 10.1161/strokeaha.112.671453

[14] Saposnik G, Barinagarrementeria F, Brown RD Jr, Bushnell CD, Cucchiara B, Cushman M, et al. Diagnosis and management of cerebral venous thrombosis: A statement for healthcare professionals from

the American Heart Association/ American Stroke Association. Stroke. 2011;**42**(4):1158-1192. DOI: 10.1161/ str.0b013e31820a8364

[15] Coutinho JM, Ferro JM, Canhão P, Barinagarrementeria F, Cantú C, Bousser MG, et al. Cerebral venous and sinus thrombosis in women. Stroke. 2009 Jul;**40**(7):2356-2361. DOI: 10.1161/strokeaha.108.543884

[16] Devasagayam S, Wyatt B, Leyden J, Kleinig T. Cerebral venous sinus thrombosis incidence is higher than previously thought: A retrospective population-based study. Stroke. 2016;**47**:2180. DOI: 10.1161/ strokeaha.116.013617

[17] Ferro JM, Canhão P, Bousser MG, et al. Cerebral vein and dural sinus thrombosis in elderly patients. Stroke. 2005;**36**:1927. DOI: 10.1161/01. str.0000177894.05495.54

[18] Zuurbier SM, Hiltunen S, Lindgren E, et al. Cerebral venous thrombosis in older patients. Stroke. 2018;**49**:197. DOI: 10.1161/ strokeaha.117.019483

[19] deVeber G, Andrew M, Adams C, et al. Cerebral sinovenous thrombosis in children. The New England Journal of Medicine. 2001;**345**:417. DOI: 10.1056/ nejm200108093450604

[20] Marjot T, Yadav S, Hasan N, Bentley P, Sharma P. Genes associated with adult cerebral venous thrombosis. Stroke. 2011;**42**(4):913. DOI: 10.1161/ strokeaha.110.602672

[21] Lüdemann P, Nabavi DG, Junker R, Wolff E, Papke K, Buchner H, et al. Factor V Leiden mutation is a risk factor for cerebral venous thrombosis: A case-control study of 55 patients. Stroke. 1998;**29**(12):2507-2510. DOI: 10.1161/01. str.29.12.2507

[22] Weih M, Junge-Hülsing J, Mehraein S, Ziemer S, Einhäupl KM. Hereditary thrombophilia with ischemiC stroke and sinus thrombosis. Diagnosis, therapy and meta-analysis. Der Nervenarzt. 2000;**71**(12):936-945. DOI: 10.1007/s001150050690

[23] Biousse V, Conard J, Brouzes C, Horellou MH, Ameri A, Bousser MG. Frequency of the 20210 G –> a mutation in the 3′-untranslated region of the prothrombin gene in 35 cases of cerebral venous thrombosis. Stroke. 1998;**29**(7):1398-1400. DOI: 10.1161/01. str.29.7.1398

[24] Reuner KH, Ruf A, Grau A, Rickmann H, Stolz E, Jüttler E, et al. Prothrombin gene G20210 –> a transition is a risk factor for cerebral venous thrombosis. Stroke. 1998;**29**(9):1765-1769. DOI: 10.1161/01.str.29.9.1765

[25] Lauw MN, Barco S, Coutinho JM, Middeldorp S. Cerebral venous thrombosis and thrombophilia: A systematic review and meta-analysis. Seminars in Thrombosis and Hemostasis. 2013 Nov;**39**(8):913-927. DOI: 10.1055/s-0033-1357504

[26] Hillier CE, Collins PW, Bowen DJ, Bowley S, Wiles CM. Inherited prothrombotic risk factors and cerebral venous thrombosis. QJM. 1998;**91**(10):677-680. DOI: 10.1093/ qjmed/91.10.677

[27] Gouveia LO, Canhão P. MTHFR and the risk for cerebral venous thrombosis--a meta-analysis. Thrombosis Research. 2010;**125**(4):e153-e158. DOI: 10.1016/j.thromres.2009.10.019

[28] Gogu AE, Jianu DC, Dumitrascu V, Ples H, Stroe AZ, Docu Axelerad D, et al. MTHFR gene polymorphisms and cardiovascular risk Factors,Clinical-imagistic features and outcome in

cerebral venous sinus thrombosis. Brain Sciences. 2021;**11**(1):1-16. Article ID (number) 23. DOI: 10.3390/brainsci11010023

[29] Gogu AE, Motoc AG, Stroe AZ, Docu Axelerad A, Docu Axelerad D, Petrica L, et al. Plasminogen activator Inhibitor-1 (PAI-1) gene polymorphisms associated with cardio-vascular risk factors involved in cerebral venous sinus thrombosis. Metabolites. 2021;**11**(5):1-13. Article ID (number)266. DOI: 10.3390/metabo11050266

[30] Lee MK, Ng SC. Cerebral venous thrombosis associated with antithrombin III deficiency. Australian and New Zealand Journal of Medicine. 1991;**21**(5):772-773. DOI: 10.1111/j.1445-5994.1991.tb01388.x

[31] Deschiens MA, Conard J, Horellou MH, Ameri A, Preter M, Chedru F, et al. Coagulation studies, factor V Leiden, and anticardiolipin antibodies in 40 cases of cerebral venous thrombosis. Stroke. 1996;**27**(10):1724-1730. DOI: 10.1161/01.str.27.10.1724

[32] Duman T, Uluduz D, Midi I, Bektas H, Kablan Y, Goksel BK, et al. A Multicenter study of 1144 patients with cerebral venous thrombosis: The VENOST study. Journal of Stroke and Cerebrovascular Diseases. 2017;**26**(8):1848. DOI: 10.1016/j.jstrokecerebrovasdis.2017.04.020

[33] Ferro JM, Canhão P. Cerebral venous sinus thrombosis: Update on diagnosis and management. Current Cardiology Reports. 2014;**16**(9):523. DOI: 10.1007/s11886-014-0523-2

[34] Bousser MG, Crassard I. Cerebral venous thrombosis, pregnancy and oral contraceptives. Thrombosis Research. 2012;**130**(Suppl 1):S19-S22. DOI: 10.1016/j.thromres.2012.08.264

[35] Cantu C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium. Review of 67 cases. Stroke. 1993;**24**(12):1880-1884. DOI: 10.1161/01.str.24.12.1880

[36] Lanska DJ, Kryscio RJ. Stroke and intracranial venous thrombosis during pregnancy and puerperium. Neurology. 1998;**51**(6):1622-1628. DOI: 10.1212/wnl.51.6.1622

[37] Kashkoush AI, Maa H, Agarwal N, Panczykowski D, Tonetti D, Weiner GM, et al. Cerebral venous sinus thrombosis in pregnancy and puerperium: A pooled, systematic review. Journal of Clinical Neuroscience. 2017;**39**:P9-P15. DOI: 10.1016/j.jocn.2017.02.046

[38] Martinelli I, Sacchi E, Landi G, Taioli E, Duca F, Mannucci PM. High risk of cerebral-vein thrombosis in carriers of a prothrombin-gene mutation and in users of oral contraceptives. The New England Journal of Medicine. 1998;**338**:1793-1797. DOI: 10.1056/nejm199806183382502

[39] de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of cerebral sinus thrombosis in oral contraceptive users and in [correction of who are carriers of hereditary prothrombotic conditions]. The cerebral venous sinus thrombosis study group. BMJ. 1998;**316**(7131):589-592. DOI: 10.1136/bmj.316.7131.589

[40] Zuurbier SM, Arnold M, Middeldorp S, et al. Risk of cerebral venous thrombosis in obese women. JAMA Neurology. 2016;**73**(5):579-584. DOI: 10.1001/jamaneurol.2016.0001

[41] Dentali F, Crowther M, Ageno W. Thrombophilic abnormalities, oral contraceptives, and risk of cerebral vein thrombosis: A meta-analysis. Blood. 2006;**107**(7):2766-2773. DOI: 10.1182/blood-2005-09-3578

[42] Knox AM, Brophy BP, Sage MR. Cerebral venous thrombosis in association with hormonal supplement therapy. Clinical Radiology. 1990;**41**(5):355-357. DOI: 10.1016/s0009-9260(05)81703-9

[43] Godeneche G, Gaillard N, Roy L, Mania A, Tondeur S, Chomel JC, et al. JAK2 V617F mutation associated with cerebral venous thrombosis: A report of five cases. Cerebrovascular Diseases. 2010;**29**(2):206-209. DOI: 10.1159/000267281

[44] Baldini T, Asioli GM, Romoli M, Carvalho Dias M, Schulte EC, Hauer L, et al. Cerebral venous thrombosis and severe acute respiratory syndrome coronavirus-2 infection: A systematic review and meta-analysis. European Journal of Neurology. 2021;**28**(10):3478-3490. DOI: 10.1111/ene.14727

[45] European Medicines Agency safety committee report. Available from: https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood [Accessed: 14, April 2021]

[46] Thakur KT, Tamborska A, Wood GK, McNeill E, David Roh D, Akpan IJ, et al. Clinical review of cerebral venous thrombosis in the context of COVID-19 vaccinations: Evaluation, management, and scientific questions. Journal of the Neurological Sciences. 2021;**427**:117532. DOI: 10.1016/j.jns.2021.117532

[47] Perry RJ, Tamborska A, Singh B, Craven B, Marigold R, Arthur-Farraj P, et al. Cerebral venous thrombosis after vaccination against COVID-19 in the UK: A multicenter cohort study. Lancet. 2021;**398**:1147-1156. DOI: 10.1016/s0140-6736(21)01608-1

[48] Pavord S, Scully M, Hunt BJ, Lester W, Bagot C, Craven B, et al. Clinical features of vaccine-induced immune thrombocytopenia and thrombosis. The New England Journal of Medicine. 2021;**385**(18):1680-1689. DOI: 10.1056/nejmoa2109908

[49] Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, EichingerS.Thromboticthrombocytopenia after ChAdOx1 nCov-19 vaccination. The New England Journal of Medicine. 2021;**384**(22):2092-2101. DOI: 10.1056/NEJMoa2104840

[50] Dobbs TD, Barber ZE, Squier WL, Green AL. Cerebral venous sinus thrombosis complicating traumatic head injury. Journal of Clinical Neuroscience. 2012;**19**(7):1058-1059. DOI: 10.1016/j.jocn.2012.01.002

[51] Schaller B, Graf R. Cerebral venous infarction-the pathophysiological concept. Cerebrovascular Diseases. 2004;**18**(3):179-188. DOI: 10.1159/000079939

[52] Gotoh M, Ohmoto T, Kuyama H. Experimental study of venous circulatory disturbance by dural sinus occlusion. Acta Neurochirurgica. 1993;**124**(2-4):120-126. DOI: 10.1007/bf01401133

[53] Lövblad KO, Bassetti C, Schneider J, Guzman R, El-Koussy M, Remonda L. Schroth G SO diffusion-weighted mr in cerebral venous thrombosis. Cerebrovascular Diseases. 2001;**11**(3):169-176. DOI: 10.1159/000047634

[54] Bousser MG, Chiras J, Bories J, Castaigne P. Cerebral venous thrombosis-a review of 38 cases. Stroke. 1985;**16**(2):199-213. DOI: 10.1161/01.str.16.2.199

[55] Ichord RN, Benedict SL, Chan AK, et al. Paediatric cerebral sinovenous thrombosis: Findings of the international

paediatric stroke study. Archives of Disease in Childhood. 2015;**100**:174. DOI: 10.1136/archdischild-2014-306382

[56] Biousse V, Ameri A, Bousser MG. Isolated intracranial hypertension as the only sign of cerebral venous thrombosis. Neurology. 1999;**53**(7):1537. DOI: 10.1212/wnl.53.7.1537

[57] Lopes MG, Ferro J, Pontes C, et al. Headache and cerebral venous thrombosis. Cephalalgia. 2000;**20**:292

[58] Cumurciuc R, Crassard I, Sarov M, et al. Headache as the only neurological sign of cerebral venous thrombosis: A series of 17 cases. Journal of Neurology, Neurosurgery, and Psychiatry. 2005;**76**:1084-1087. DOI: 10.1136/jnnp.2004.056275

[59] de Bruijn SF, Stam J, Kappelle LJ. Thunderclap headache as first symptom of cerebral venous sinus thrombosis. CVST study group. Lancet. 1996;**348**(9042):P1623-P1625. DOI: 10.1016/s0140-6736(96)07294-7

[60] Jianu DC, Jianu SN, Dan TF, Iacob N, Munteanu G, Motoc AGM, et al. Diagnosis and Management of Mixed Transcortical Aphasia due to multiple predisposing factors, including postpartum and severe inherited thrombophilia, affecting multiple cerebral venous and Dural sinus thrombosis: Case report and literature review. Diagnostics. 2021;**11**(8):1425. DOI: 10.3390/diagnostics11081425

[61] Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F. Early seizures in cerebral vein and Dural sinus thrombosis risk factors and role of Antiepileptics. Stroke. 2008;**39**:1152-1158. DOI: 10.1161/strokeaha.107.487363

[62] Ferro JM, Correia M, Rosas MJ, Pinto AN, Neves G, the Cerebral Venous Thrombosis Portuguese Collaborative Study Group [VENOPORT]. Seizures in cerebral vein and dural sinus thrombosis. Cerebrovascular Diseases. 2003;**15**:78-83. DOI: 10.1159/000067133

[63] Lancon JA, Killough KR, Tibbs RE, et al. Spontaneous dural sinus thrombosis in children. Pediatric Neurosurgery. 1999;**30**(1):23-29. DOI: 10.1159/000028755

[64] Ferro JM, Correia M, Pontes C, et al. Cerebral vein and dural sinus thrombosis in Portugal: 1980-1998. Cerebrovascular Diseases. 2001;**11**(3):177-182. DOI: 10.1159/000047635

[65] Damak M, Crassard I, Wolff V, Bousser MG. Isolated lateral sinus thrombosis a series of 62 patients. Stroke. 2009;**40**:476-481. DOI: 10.1161/strokeaha.107.509711

[66] Jianu DC, Jianu SN, Motoc AGM, Poenaru M, Petrica L, Vlad A, et al. Diagnosis and management of a young woman with acute isolated lateral sinus thrombosis. Romanian Journal of Morphology and Embryology. 2017;**58**(4):1515-1518 www.rjme.ro

[67] Waldvogel D, Mattle HP, Sturzenegger M, Schroth G. Pulsatile tinnitus--a review of 84 patients. Journal of Neurology. 1998;**245**(3):137-142. DOI: 10.1007/s004150050193

[68] Sakaida H, Kobayashi M, Ito A, Takeuchi K. Cavernous sinus thrombosis: Linking a swollen red eye and headache. Lancet. 2014;**384**(9946):928. DOI: 10.1016/s0140-6736(14)61404-5

[69] Ebright JR, Pace MT, Niazi AF. Septic thrombosis of the cavernous sinuses. Archives of Internal Medicine. 2001;**161**(22):2671-2676. DOI: 10.1001/archinte.161.22.2671

[70] Jacobs K, Moulin T, Bogousslavsky J, et al. The stroke syndrome of cortical vein thrombosis. Neurology. 1996;**47**(2):376-382. DOI: 10.1212/wnl.47.2.376

[71] Lacour JC, Ducrocq X, Anxionnat R, et al. Thrombosis of deep cerebral veins in form adults: Clinical features and diagnostic approach. Revue Neurologique (Paris). 2000;**156**(10):851-857

[72] van den Bergh WM, van der Schaaf I, van Gijn J. The spectrum of presentations of venous infarction caused by deep cerebral vein thrombosis. Neurology. 2005;**65**(2):192-196. DOI: 10.1212/01.wnl.0000179677.84785.63

[73] Pekçevik Y, Pekçevik R. Why should we report posterior fossa emissary veins? Diagnostic and Interventional Radiology. 2014;**20**(1):78-81. DOI: 10.5152/dir.2013.13203

[74] Jianu DC, Jianu SN, Dan TF, Motoc AGM, Poenaru M. Pulsatile tinnitus caused by a dilated left petrosquamosal sinus. Romanian Journal of Morphology and Embryology. 2016;**57**(1):319-322 www.rjme.ro

[75] Kuehnen J, Schwartz A, Neff W, Hennerici M. Cranial nerve syndrome in thrombosis of the transverse/sigmoid sinuses. Brain. 1998;**121**(Pt 2):381-388. DOI: 10.1093/brain/121.2.381

[76] Ferro JM, Bousser M-G, Canhãoa P, Coutinho JM, Crassard I, Dentali F, 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**(10):1203-1213. DOI: 10.1111/ene.13381

[77] Dentali F, Squizzato A, Marchesi C, et al. D-dimer testing in the diagnosis of cerebral vein thrombosis: A systematic review and a meta-analysis of the literature. Journal of Thrombosis and Haemostasis. 2012;**10**(4):582-589. DOI: 10.1111/j.1538-7836.2012.04637.x

[78] Meng R, Wang X, Hussain M, et al. Evaluation of plasma D-dimer plus fibrinogen in predicting acute CVST. International Journal of Stroke. 2014;**9**(2):166-173. DOI: 10.1111/ijs.12034

[79] Canhão P, Abreu LF, Ferro JM, et al. Safety of lumbar puncture in patients with cerebral venous thrombosis. European Journal of Neurology. 2013;**20**(7):1075-1080. DOI: 10.1111/ene.12136

[80] Rizzo L, Crasto SG, Rudà R, et al. Cerebral venous thrombosis: Role of CT, MRI and MRA in the emergency setting. La Radiologia Medica. 2010;**115**(2):313-325. DOI: 10.1007/s11547-010-0493-4

[81] Qu H, Yang M. Early imaging characteristics of 62 cases of cerebral venous sinus thrombosis. Experimental and Therapeutic Medicine. 2013;**5**(1):233-236. DOI: 10.3892/etm.2012.796

[82] Boukobza M, Crassard I, Bousser MG, Chabriat H. MR imaging features of isolated cortical vein thrombosis: Diagnosis and follow-up. American Journal of Neuroradiology. 2009;**30**(2):344-348. DOI: 10.3174/ajnr.a1332

[83] Dan TF, Jianu SN, Iacob N, Motoc AGM, Munteanu G, Baloi A, et al. Management of an old woman with cavernous sinus thrombosis with two different mechanisms: Case report and review of the literature. Romanian Journal of Morphology and Embryology. 2020;**61**(4):1329-1334. DOI: 10.47162/RJME.61.4.35

[84] Buyck P-J, De Keyzer F, Vanneste D, Wilms G, Thijs V, Demaerel P. CT density

measurement and H:H ratio are useful in diagnosing acute cerebral venous sinus thrombosis. American Journal of Neuroradiology. 2013;**34**(8):1568-1572. DOI: 10.3174/ajnr.a3469

[85] Poon CS, Chang J-K, Swarnkar A, Johnson MH, Wasenko J. Radiologic diagnosis of cerebral venous thrombosis: Pictorial review. American Journal of Roentgenology. 2007;**189**(Suppl 6):S64-S75. DOI: 10.2214/ajr.07.7015

[86] Virapongse C, Cazenave C, Quisling R, et al. The empty delta sign: Frequency and significance in 76 cases of dural sinus thrombosis. Radiology. 1987;**162**(3):779-785. DOI: 10.1148/radiology.162.3.3809494

[87] Majoie CB, van Straten M, Venema HW, den Heeten GJ. Multisection CT venography of the dural sinuses and cerebral veins by using matched mask bone elimination. AJNR. American Journal of Neuroradiology. 2004;**25**:787 PMID: 15140721

[88] Khandelwal N, Agarwal A, Kochhar R, et al. Comparison of CT venography with MR venography in cerebral sinovenous thrombosis. AJR. American Journal of Roentgenology. 2006;**187**:1637. DOI: 10.2214/ajr.05.1249

[89] Leach JL, Fortuna RB, Jones BV, Gaskill-Shipley MF. Imaging of cerebral venous thrombosis: Current techniques, spectrum of findings, and diagnostic pitfalls. Radiographics. 2006;**26**(Suppl. 1):S19. DOI: 10.1148/rg.26si055174

[90] Rodallec MH, Krainik A, Feydy A, et al. Cerebral venous thrombosis and multidetector CT angiography: Tips and tricks. Radiographics. 2006;**26**(Suppl. 1):S5. DOI: 10.1148/rg.26si065505

[91] Dormont D, Anxionnat R, Evrard S, et al. MRI in cerebral venous thrombosis. Journal of Neuroradiology. 1994;**21**:81 PMID: 8014661

[92] Isensee C, Reul J, Thron A. Magnetic resonance imaging of thrombosed dural sinuses. Stroke. 1994;**25**:29. DOI: 10.1161/01.str.25.1.29

[93] Fellner FA, Fellner C, Aichner FT, Mölzer G. Importance of T2*-weighted gradient-echo MRI for diagnosis of cortical vein thrombosis. European Journal of Radiology. 2005;**56**:235. DOI: 10.1016/j.ejrad.2005.05.010

[94] Selim M, Fink J, Linfante I, et al. Diagnosis of cerebral venous thrombosis with echo-planar T2*-weighted magnetic resonance imaging. Archives of Neurology. 2002;**59**:1021. DOI: 10.1001/archneur.59.6.1021

[95] Mittal S, Wu Z, Neelavalli J, Haacke EM. Susceptibility weighted imaging: Technical aspects and clinical applications. Part 2. AJNR. American Journal of Neuroradiology. 2009;**30**:232-252. DOI: 10.3174/ajnr.A1461

[96] Favrole P, Guichard JP, Crassard I, et al. Diffusion-weighted imaging of intravascular clots in cerebral venous thrombosis. Stroke. 2004;**35**:99. DOI: 10.1161/01.str.0000106483.41458.af

[97] Meckel S, Reisinger C, Bremerich J, Damm D, Wolbers M, Engelter S, et al. Cerebral venous thrombosis: Diagnostic accuracy of combined, dynamic and static, contrast-enhanced 4D MR venography. AJNR. American Journal of Neuroradiology. 2010;**31**:527-535. DOI: 10.3174/ajnr.A1869

[98] Pallewatte AS, Tharmalingam T, Liyanage N. Anatomic variants and artefacts in non-enhanced MRV - potential pitfalls in diagnosing cerebral venous sinus thrombosis (CVST). SLJR.

2016;**2**(1):40-46. DOI: 10.4038/sljr.v2i1.23

[99] Wetzel SG, Kirsch E, Stock KW, et al. Cerebral veins: Comparative study of CT venography with intraarterial digital subtraction angiography. AJNR. American Journal of Neuroradiology. 1999;**20**:249 PMCID: PMC7056122