Cerebral Venous Thrombosis

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Abstract

Cerebral venous thrombosis (CVT) is a rare form of stroke that often affects younger age groups, especially reproductive age group females. CVT is a potentially fatal neurological condition that can be frequently overlooked due to the vague nature of its clinical and radiological presentation. Headache is the most common presenting symptom. However, a wide range of symptoms can be present and the symptom onset can be acute, subacute, or chronic. Neuroimaging is mandatory in cases where CVT is suspected. Both magnetic resonance venography and computed tomography venography can confirm a diagnosis of CVT. Anticoagulation with low-molecular-weight heparin is the mainstay of treatment. Intracranial hemorrhage is not considered a contraindication to the use of anticoagulants in CVT. Endovascular intervention is still controversial but can be a treatment option for patients with neurological deterioration or thrombus progression, despite the use of anticoagulation or with development of new or worsening intracerebral hemorrhage. Patients with CVT have an increased risk of recurrence of CVT and other types of venous thromboembolism. This review provides an overview of the epidemiology, diagnosis, and treatment of CVT in adults. Commentary about increased presentation of CVT in patients with coronavirus disease 2019 (COVID-19), or after immunization against COVID-19, is also provided.

Keywords

- cerebral venous thrombosis
- anticoagulants
- endovascular intervention
- cerebral hemorrhage

Cerebral venous thrombosis (CVT), with occlusion of one or more cerebral veins or dural venous sinuses, is uncommon and may lead to venous infarction and hemorrhage. In contrast to both venous thromboembolism (VTE) with other locations and arterial stroke, younger and female patients are more commonly affected (up to three times more often than men).[1,2]

Headache, seizures, or focal neurological deficits are the most common presenting symptoms; however, patients can present with a wide range of signs and symptoms. Due to this variability in clinical manifestations, and the rarity of the condition, CVT can be difficult to diagnose. Given the broad spectrum of causes and presenting scenarios, CVT may be encountered not only by neurologists and neurosurgeons but also by emergency physicians, internists, oncologists, hematologists, obstetricians, pediatricians, and general practitioners. CVT that cause venous infarctions represents approximately 0.5% of all cerebral infarctions.[4]

CVT shares many of the same characteristics as other VTE, and the evidence-based recommendations for other VTE are widely used for CVT. Why CVT is so rare compared with VTE located elsewhere in the body is unknown.

In this review, an overview of the epidemiology, diagnosis, and treatment of CVT in adults is given.

Anatomy

The venous systems of the brain consist of cerebral veins and cerebral sinus veins. Both lack valves and muscular tissue. They are divided into a superficial and a deep system according to their drainage relative to the ventricles. The deep veins typically originate in white matter as medullary veins and drain into subependymal veins. The superficial veins are located on the surface of the brain, run along the sulci, and do not follow cerebral arterial territories. Most

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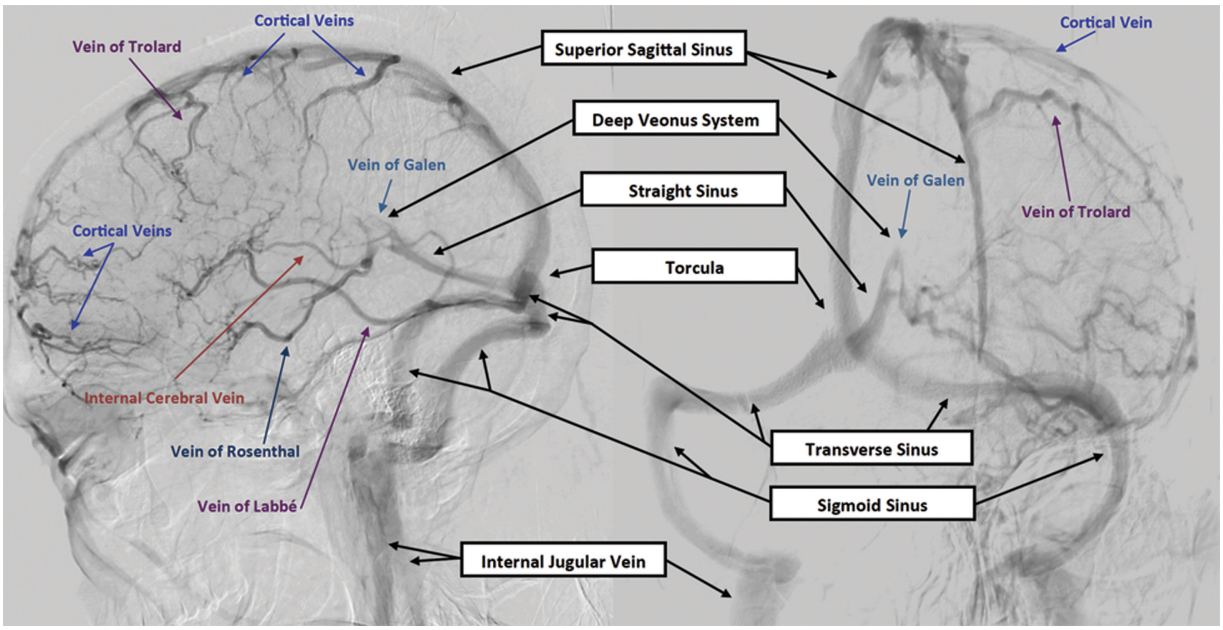

Fig. 1 Digital subtraction angiography demonstrating the anatomy of the venous system of the brain. The images are in venous phase after contrast injection in the left internal carotid artery with lateral projection to the left and frontal projection to the right. The major cerebral venous sinuses and major superficial and deep veins are visible. For demonstration of the sylvian vein see ►**Fig. 5**.

superficial and deep cerebral veins drain to cerebral sinus veins. The sinus veins are located between the endosteal and meningeal layers of the dura mater. They run along the edges of the dura mater with the largest and most important following falx and the tentorium. Until recently, the superior sagittal sinus has been considered the most important draining pathway for cerebrospinal fluid (CSF) through the arachnoid villi. Advances in the understanding of the glymphatic system have demonstrated outflow along cranial nerves, through meningeal lymphatic vessels and from the spine to be the main outflow routes of CSF.[5–7] The largest proportion of blood from both the superficial and deep venous systems eventually drains into the internal jugular veins (►**Fig. 1**). Other outputs are emissary veins, which run through a large number of foramina in the skull and venous plexus in the foramen magnum.

Epidemiology

In recent population-based studies, the incidence of CVT was identified as 1.32 to 1.75 per 100,000/year[4,8–10] which is higher than earlier studies.[3,11] The reason why more cases are diagnosed than previously, is probably because there is more attention to the condition and due to use of better radiological diagnostics. CVT is most common at ages 20 to 50 years whereas less than 1 out of 10 individuals with CVT are older than 65 years.[1]

Risk Factors

Multiple risk factors are associated with CVT. At least one risk factor can be identified in 85% of affected adults.[12,13] Prior medical conditions (e.g., thrombophilia, inflammatory bowel disease), transient situations (e.g., pregnancy, dehydration, infection), selected medications (e.g., oral contraceptives), and unpredictable events (e.g., head trauma) comprise some predisposing conditions. Many of these conditions are risk factors for VTE in general,[2] such as chronic inflammatory disorders including vasculitis, myeloproliferative neoplasms, other malignancies, and genetic thrombophilia. Furthermore, there are specific conditions that increase the CVT risk, such as infections in head and neck, head trauma, neurosurgical interventions, lumbar puncture, and arteriovenous malformations[2,14] (►**Table 1**). The relationship between CVT and coronavirus disease 2019 (COVID-19) and vaccines are commented on in a separate paragraph.

The female preponderance can largely be explained by sex-specific risk factors of estrogen-containing oral contraceptives, pregnancy, and puerperium.[3,15,16] Women who use oral contraceptives have a sixfold increase in risk of CVT. However, the risk is even higher in women with obesity using oral contraceptives.

The risk factors vary between countries. In Mediterranean and Middle Eastern countries, CVT is more often caused by Behçet than in other countries.[17–19] In large international registries and European countries, risk factors including dehydration, pregnancy, and puerperium are more seldom reported than in Asian and Middle Eastern countries.[2]

Pathophysiology

The pathophysiological mechanisms in CVT are not fully understood. The current understanding of the imbalance in prothrombotic and thrombolytic mechanisms that lead to thrombus formation is based partly on animal models.[20] Thrombosis of the cerebral veins lead to increased capillary

Table 1 Risk factors for cerebral venous thrombosis

Risk factor	Description
Sex-specific	Estrogen-containing oral contraceptives, pregnancy, puerperium, estrogen-containing hormone replacement therapy
Mechanical	Surgical interventions, lumbar puncture, jugular vein catheterization, head trauma
Infections	Intracranial: meningitis Systemic: human immunodeficiency virus (HIV), tuberculosis, COVID-19, and sepsis Local: otitis media, mastoiditis, oral, sinus, head, and neck infections
Intracranial defects	Tumor, spontaneous intracranial hypotension, arteriovenous malformations, dural fistulas, venous anomalies
Hematological	Essential thrombocythemia, myeloproliferative neoplasms, primary and secondary polycythemia, anemia including paroxysmal nocturnal hemoglobinuria
Hereditary thrombophilia	Factor V Leiden mutation, G20210A prothrombin gene mutation, antithrombin III deficiency, and protein C and S deficiency, homocysteinemia caused by gene mutations in methylenetetrahydrofolate reductase
Vasculitis	Systemic lupus erythematosus, Sjøgren's syndrome, temporal arteritis, antiphospholipid syndrome, thromboangiitis obliterans, Wegener's granulomatosis, Behcet's disease
Systemic	Cancer, inflammatory bowel disease, thyroid disease, nephrotic syndrome, sarcoidosis, dehydration, obesity, antiphospholipid syndrome
Drugs	Hormone therapy (tamoxifen, androgens), chemotherapy (cyclosporine, l-asparaginase)

and venular pressure. The brain's venous system with its extensive anastomoses (►**Fig. 1**) can provide collateral circulation to compensate temporarily for the increased pressure. However, when the collateral capacity becomes insufficient, the cerebral perfusion is reduced. Consequently, the continued venous and capillary pressure increase may cause disruption of the blood-brain barrier, vasogenic edema, and venous and capillary rupture that can lead to hemorrhage. The reduction in cerebral perfusion pressure and cerebral blood can lead to failure of energy metabolism with intracellular entry of water from failure of the $Na^+/K+$-ATPase pump and consequent cytotoxic edema[21] (►**Fig. 2**). Parenchymal lesions with venous infarctions in CVT are associated with severe clinical manifestation and poor outcome, particularly when hemorrhage is present. Cortical vein thrombosis correlates with poor clinical outcome and parenchymal lesions.[22] It has been shown in animal models that parenchymal lesions can also occur without cortical vein occlusions.[23,24] The parenchymal lesions that occur in approximately 60% of patients with CVT, differ considerably from those in arterial stroke crossing arterial boundaries and with hemorrhagic components in two of three cases.[2] Approximately 30 to 50% of the patients with CVT have intracerebral hemorrhage, which can range from a small juxtacortical hemorrhage to large space-occupying lesions.

The new discoveries of dura, and especially the dural sinuses as an important connection between the central nervous system and the peripheral immune system[25,26] are interesting in discussing cerebral sinus venous thrombosis related to infections and inflammatory disorders. There are a large number of connections between dura mater and hematopoietic bone marrow overlying the dural sinuses where antigens are presented for circulating T cells.[27]

Clinical Presentation

The diagnosis of CVT can be difficult.[21] It is not uncommon for CVT to be diagnosed so late, that serious complications

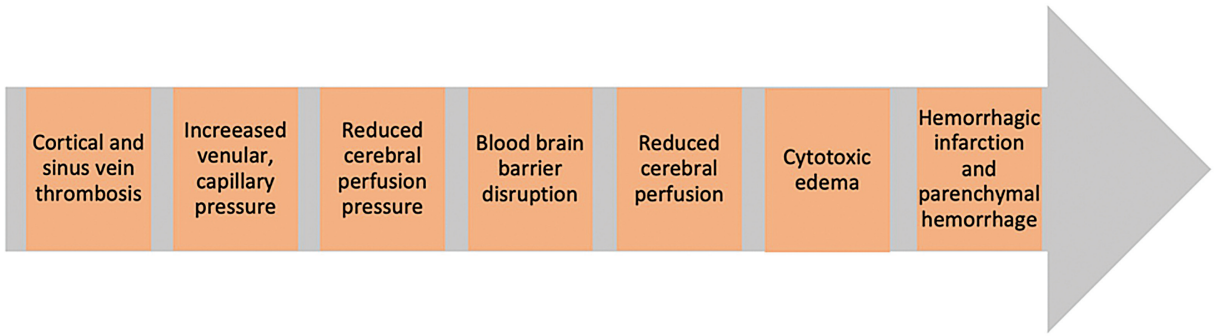

Fig. 2 Pathophysiology of cerebral venous thrombosis. CSF, cerebrospinal fluid.

may have already arisen. The onset of symptoms is usually subacute with development over 2 to 30 days.[11] The presentation of symptoms is highly variable. CVT patients are sometimes diagnosed in the outpatient clinic with a long-standing history of headache whereas others can be admitted in comatose state to the emergency room.

Most patients have symptoms and signs of CVT, which can be grouped into four main categories. First, the most frequent ones are isolated intracranial hypertension syndrome with headache often accompanied by nausea, papilledema, decreased visual acuity, and tinnitus. Second, focal syndrome caused by thrombosis of the superficial venous system and parenchymal lesions with infarction and hemorrhage generally present with focal neurological deficits, often in combination with seizures. Third, thrombosis of the deep venous system with bilateral edema of the basal ganglia and thalami, which typically presents with mental status disorder, gaze palsy, diffuse encephalopathy, or coma.[9] Less frequent presentation syndromes are cases that affect the cavernous sinus, presenting with orbital pain, chemosis, proptosis, and ophthalmoplegias.[8]

Headache is the most prevalent symptom occurring in 60 to 90% of CVT patients and is usually the first manifesting symptom.[28,29] Although CVT is rare, the condition should be suspected in everyone with newly unexplained severe headache. CVT headache has a highly variable presentation without an obvious pattern and should be identified as soon as possible in the patient's presentation.[30] The character of the headache may be pulsating, pressing, or thunderclap type, and either unilateral or bilateral. The headache in CVT can be difficult to differentiate from primary headache disorders but some clues include subacute onset, diffuse and throbbing quality of the pain, phono- and photophobia, neurological deficits, worsening with Valsalva maneuvers, and signs of intracranial hypertension such as papilledema.[31]

Although headache in CVT is considered as a symptom of increased intracranial pressure, there is limited literature to explain the mechanism. Mechanical stretching of nerve fibers in the walls of occluded venous sinuses due to venous volume expansion and dilatation of the sinus and cortical and spinal veins may cause headache.[24] Since the dura surrounding the sinuses is innervated by the trigeminal nerve, the trigeminovascular system, may also be activated and cause migrainous headache.[26] Additionally, cortical infarcts and increased intracranial pressure that can occur secondary to the venous thrombosis may also cause headache.[24]

Focal or generalized seizures occur in 20 to 40% of patients within the 2 weeks of diagnosis, which is a noticeably higher incidence than in arterial ischemic stroke (2–9%) or intracerebral hemorrhage (8–14%).[32–34] Eight of 10 people with acute symptomatic seizures have seizures before the diagnosis has been established.[2] CVT patients can also present as status epilepticus, or they may develop status epilepticus, particularly in severe forms with supratentorial and multiple hemorrhagic lesions.[35] Papilledema is reported in 30 to 60%

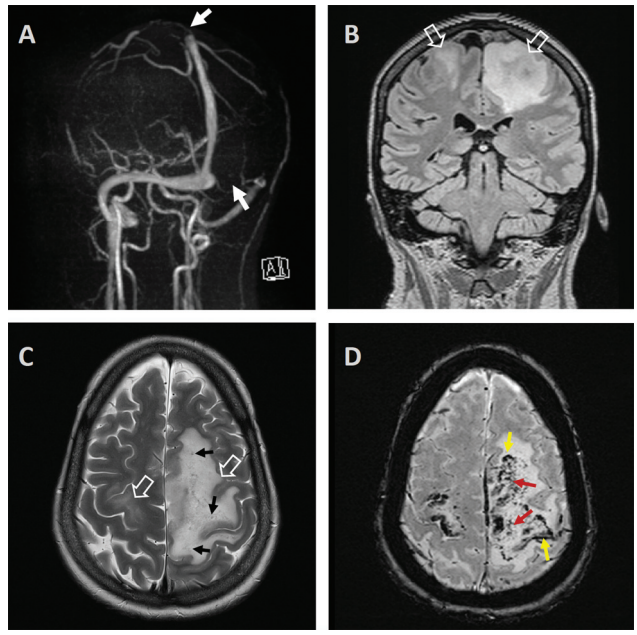

Fig. 3 Magnetic resonance images demonstrate cerebral venous thrombosis and venous infarctions. (**A**) Lack of flow signal from thrombosis in the superior sagittal sinus and the left transverse sinus (white arrows) is evident on the three-dimensional (3D) model generated from a phase contrast venography. (**B**) High signal from edema in venous infarctions (open white arrows) is demonstrated on the coronal fluid-attenuated inversion recovery (FLAIR) sequence. (**C**) High signal from edema (open white arrows) and low signal from microhemorrhages (black arrows) in venous infarctions can be seen on this axial T2 turbo spin echo sequence. (**D**) Signal loss from deoxygenated stagnant venous blood (yellow arrows) and from microhemorrhages (red arrows) on this thin (1.6 mm) axial minimum intensity projection (MinIP) reconstruction from susceptibility weighted imaging (SWI) sequence.

of patients,[2] and 10 to 20% of patients have altered consciousness at the time of diagnosis.[12,19]

Elderly patients with CVT usually have a distinctive clinical presentation, with mental status and alertness disturbances being common, whereas headache and isolated intracranial hypertension is uncommon.[1] Approximately half of patients with CVT have an intracerebral hemorrhage at presentation (►**Fig. 3**).[12]

Diagnosis

Laboratory Tests

There are still no validated pretest clinical probability scores or laboratory tests that can confidently rule out CVT. D-dimer is a potentially useful diagnostic tool before imaging examination. However, false negatives can occur, particularly in patients with isolated headache or prolonged duration of symptoms beyond 1 week.[31] Routine laboratory tests including complete blood count, coagulation profile, and metabolic panel can contribute to the identification of associated conditions.

Imaging

Neuroimaging is mandatory in cases where CVT is suspected.[36] Magnetic resonance venography (MRV) and

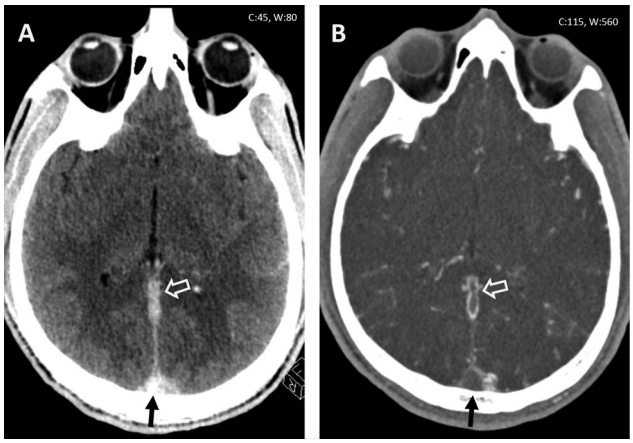

Fig. 4 Noncontrast computed tomography (NCCT) in (**A**) and computed tomography venography (CTV) in (**B**) show evidence of thrombosis in superior sagittal sinus (black arrow) and vein of Galen (open white arrow). High attenuation is evident in the thrombus on the NCCT. The empty delta sign with a triangular filling defect in superior sagittal sinus is clearly demonstrated on the CTV.

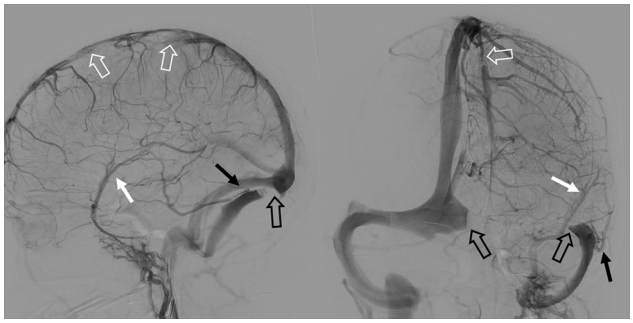

Fig. 5 Digital subtraction angiography in venous phase (same patient as in ►**Fig. 3**) after contrast injection in the left internal carotid artery with lateral projection to the left and frontal projection to the right, demonstrates a filling defect in the left transverse sinus (open black arrows) and partly filling defects in the superior sagittal sinus (open white arrows). Thrombus in the vein of Labbé is evident (closed black arrow). Anastomoses between the vein of Labbé and the sylvian vein (closed white arrow) can be seen.

computed tomography (CT) venography (CTV) are adequate for diagnosis of CVT (►**Figs. 3**,**4**,**5**).[23] Whereas MR imaging (MRI) is clearly superior for the visualization of brain parenchymal lesion, CT is easier to access in most hospitals.

Noncontrast CTV can demonstrate classic direct signs of CVT in approximately 1 of 4 patients, such as the characteristic clot in superior sagittal sinus and vein of Galen (►**Fig. 4**).[37] However, these typical signs are often not seen in the subacute phase and are not specific.[36] CTV provides a detailed depiction of the cerebral venous system, and enables correct identification of sinuses in approximately 99% of patients and cerebral veins in approximately 88% of patients.[34] Thrombosis can be seen as regions without contrast in the veins or sinuses. A nonopacified thrombus surrounded by a rim of contrast in the sinus wall is called the empty delta sign and is often evident in thrombosis of the superior sagittal sinus (►**Fig. 4**). The diagnostic yield of CTV alone is limited by the common presence of several anatomic variants that may mimic sinus thrombosis.[23] Signals on both T1- and T2-weighted MRI sequences are highly variable in a thrombus depending on the age of the clot and the composition of breakdown products of hemoglobin. The signal range includes the same signals as in normal venous blood. The use of T2*-weighted gradient sequences (T2*GRE) or susceptibility weighted imaging (SWI) is recommended to improve diagnostic accuracy and is especially useful to detect isolated cortical vein thrombosis.[35,36] Lack of flow dependent signal on MRV, lack of contrast enhancement, and lack of flow voids that gives high signal on T2-weighted sequences, are all signs of thrombosis in the cerebral sinuses or veins. Contrast enhancement in the thrombus is normal in chronic CVT. Edema from venous infarctions is best visualized on T2-weighted sequences as fluid-attenuated inversion recovery. Parenchymal hemorrhage is best visualized as signal loss on T2* or SWI. The brush sign is used to describe an abnormally accentuated signal drop of the subependymal and deep medullary veins in paramagnetic-sensitive MR sequences. This sign is occasionally found in CVT, especially in patients with thrombosis of the deep venous system or straight sinus. This sign probably represents increased deoxyhemoglobin and engorgement of the deep veins and is associated with clinical presentation with focal signs, more extensive thrombosis, and ipsilateral parenchymal brain lesion.[38]

Catheter angiography remains the most accurate method for diagnosis of CVT but is seldom required.[39] As catheter angiography is an invasive technique with a nonnegligible risk, a patient should only undergo this procedure when CTV or MRV are inconclusive, a dural arteriovenous fistula is suspected, or when an endovascular therapeutic intervention is planned.

Treatment

Current guidelines recommend that patients with CVT are admitted to a stroke unit and treated with either low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) followed by an oral vitamin K antagonist (VKA) for 3 to 12 months.[36] Anticoagulation is used to promote clot resolution and prevent clot expansion. Small-scale studies comparing the safety and efficacy of anticoagulation with placebo has shown a clinically favorable trend toward the use of anticoagulants in patients with CVT.[36] Direct oral anticoagulants (DOACs) have already established benefit over warfarin as a long-term treatment of symptomatic VTE, like deep vein thrombosis and pulmonary embolism, given its equal efficacy and better safety profile. Recent systematic reviews and meta-analyses have generated robust evidence regarding the safety and efficacy of DOACs in CVT and showed similar efficacy and safety compared with VKAs with better recanalization rate.[36,38] Although the lack of recommendations in guidelines, physicians recognize the benefits of DOACs also in CVT and are increasingly using DOACs instead of VKA.[39] As only a few studies used DOACs directly and the majority use LMWH or UFH before starting DOACs,[38,39] it is still recommended to use heparin when initiating anticoagulation therapy in the acute phase.[36] In

CVT, treatment of underlying conditions, such as infection and dehydration, is recommended.[37] In patients with symptomatic seizures antiepileptic treatment should be given. Especially patients with parenchymal cortical lesions have increased risk of seizures and prophylactic antiepileptic treatment can be considered.[36] A few patients have a severe presentation as encephalopathy or coma and may need intensive care.[40,41] These patients have decreased consciousness, altered mental status, bilateral or multifocal signs, and/or seizures or status epilepticus.

Endovascular treatment (EVT) of dural sinus thrombosis is increasingly being used, and can be an option in patients with neurological deterioration despite the use of anticoagulation or with development of new or worsening intracerebral hemorrhage on anticoagulation.[36] Current endovascular techniques include, but are not limited to, direct catheter thrombolysis, balloon-assisted thrombectomy, rheolytic catheter thrombectomy, aspiration thrombectomy, and stent retriever thrombectomy. Different equipment and methods are reported in a large number of case reports with highly variable grade of recanalization and outcomes.[42,43] The variation in endovascular mechanical thrombectomy techniques for CVT intervention has made a comprehensive assessment of its outcomes difficult.

EVT has been reported to have favorable results in case series, mainly for thrombectomy rather than thrombolysis,[44,45] but the studies have lacked a comparison group. A multicenter open-label, blinded endpoint, randomized trial of endovascular therapy with CVT patients having at least one risk factor for poor outcome (comatose state, mental status disorder, thrombosis of the deep venous system, or intracerebral hemorrhage) were performed at eight centers in three countries.[44] EVT plus standard medical therapy were compared with only standard medical therapy. The trial was stopped prematurely after 67 accrued patients because of futility. However, a variety of endovascular techniques were used, making conclusions uncertain.[45] Moreover, EVT may be less efficient when both cortical veins and the sinus are occluded as it only may have effect on the sinuses and not the small cortical veins.

In patients who develop clinical and radiological signs of impending herniation, decompressive surgery can be both lifesaving and result in a good functional outcome.[36] However, this approach has been studied less extensively in patients with CVT than in those with either arterial cerebral infarctions and brain edema or traumatic brain injury.[39] Furthermore, open surgical thrombectomy combined with decompressive craniectomy can be a lifesaving treatment option that can lead to favorable outcome and should be considered for treatment of refractory malignant CVT.[46,47]

Trauma and Lumbar Puncture

CVT can also have mechanical causes such as traumatic brain injury, neurosurgical procedures, and other interventions causing direct injury to the sinuses or the jugular veins.[3] Prospective trials are necessary to develop guidelines for the management of occlusive CVT in patients with severe traumatic brain injury and to determine which patient populations are likely to benefit from early initiation of therapeutic anticoagulation.

In rare cases, CVT is reported as a complication to lumbar puncture, usually in combination with coexisting predisposing conditions.[48,49] A plausible mechanism for CVT after lumbar puncture may be that low CSF pressure can cause a downward shift of the brain and traction on the cortical veins and sinuses. Deformation of the venous walls may induce thrombosis. Differentiating headache due to CVT from post-dural puncture headache may be difficult. However, headaches after lumbar puncture are usually postural and disappear when patients lie down.[31] Furthermore, these commonly resolve within a few days, whereas headaches in patients with CVT are not postural and worsen during the first stage of the disease.

Pregnancy and Puerperium

CVT occurrence during pregnancy should be treated with LMWH and continued through 6 weeks of postpartum.[50] The occurrence of CVT during pregnancy is usually not considered as a contraindication for future pregnancies.[51] However, LMWH should be administered as prophylaxis during pregnancy/puerperium for pregnant women with previous history of CVT if there are no contraindications.[51] In patients who develop CVT with oral contraceptive pills or hormone replacement therapy, only progesterone is recommended, and other forms should be stopped.[51]

COVID-19, COVID-19 Vaccines, and Other Infections

Infections can predispose to both arterial and venous thromboembolic events such as deep venous thrombosis, pulmonary embolism, myocardial infarction, and stroke. CVT is a rare event associated with COVID-19. Clinicians should consider the risk of acute CVT in patients found positive for COVID-19, especially if neurological symptoms develop.[52]

Severe cases of CVT with thrombocytopenia and anti-platelet factor 4 (PF4) antibodies have been reported to occur after vaccination with certain adenovirus vector-based vaccines against SARS-CoV-2.[52–54] Approximately half of the patients identified with thrombosis and thrombocytopenia syndrome (TTS) or vaccine-induced immune thrombotic thrombocytopenia (VITT) after COVID-19 vaccination in the early reports presented with CVT, while almost one-third of these patients do not survive.[55] New guidelines state that the anti-PF4 antibody enzyme-linked immunosorbent assay test, as normally performed for evaluation of heparin-induced thrombocytopenia, should be performed in patients presenting with CVT and thrombocytopenia after COVID-19 vaccinations to confirm TTS/VITT.[56,57] Urgent clinical and neuroimaging evaluation is essential. In patients with suspected or confirmed TTS/VITT, early intravenous immunoglobulins are indicated and heparin (UFH or LMWH) should be avoided whereas nonheparin anticoagulants are preferred. If possible, platelet transfusions should be avoided.[57]

Table 2 Key points of the present review

The cerebral veins are an unusual site of thrombosis that can easily be overlooked with a considerable risk of delayed diagnosis
Cerebral venous thrombosis (CVT) is an essential cause of stroke in younger age groups
Recommended treatment for CVT is low-molecular weight heparin followed by oral anticoagulation
Endovascular therapy (EVT) can be an option in severe cases of CVT with thrombus progression despite optimal treatment with heparin, however, more research is necessary to establish the role of EVT
Mortality among patients with CVT is 8–10%. Residual chronic symptoms are common after CVT, although 80% of patients recover without physical disability, up to 2% in recent studies.

So far, significant increase of CVT after messenger ribonucleic acid COVID-19 vaccinations have not been demonstrated.[58,59] However, as CVT is relatively rare the studies may not have been sufficiently powered to identify a small incremental risk.

Prognosis

In hospital mortality among patients with CVT in recent studies is 2 to 2%.[12,19,60] Although many of patients recover without physical disability, residual chronic symptoms are common.[12] A long-term follow-up study showed that one-third did not return to work.[61] Baseline variables associated with poor prognosis include high age, mental status disorder, comatose state, intracerebral hemorrhage, and thrombosis of the deep venous system.[1,12] The prognosis is generally good and far better than in arterial cerebral infarctions,[15] but 2-4% of patients with CVT die in the acute phase, mainly due to cerebral herniation.[16,60] About twice as many patients die within 6 months after the acute phase, most often from the underlying causes of the venous thrombosis, such as cancer. A subgroup of clinically identifiable CVT patients, approximately 1 in 10 patients, are at increased risk of adverse outcome.[12] These high-risk patients may benefit from more aggressive therapeutic interventions, but randomized clinical trials are needed. CVT during pregnancy usually has a very good prognosis.[50]

Conclusion and Future Perspectives

The key points of the present review are summarized in ►**Table 2**. More research is needed to better understand the natural course of CVT to optimize diagnosis and management of the disease. Multicenter academic collaboration is crucial to improve our knowledge of CVT. Large randomized control trials are required to provide stronger evidence for the various therapeutic interventions of CVT including the timing of DOACs and the use of EVT.

Conflict of Interest

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