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REVIEW

The changing face of cerebral venous sinus thrombosis—emerging new causes and treatments

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Abstract

Cerebral venous sinus thrombosis (CVST) is an uncommon site of venous thromboembolism. CVST more commonly affects younger people and women, in stark contrast to other forms of venous thrombosis in which incidence increases with age and overall affects men. Traditional risk factors for the development of CVST include endogenous and exogenous estrogen (combined oral contraceptives and pregnancy and the puerperium), thrombophilias, and rare hematologic disorders. New and emerging risk factors include obesity, polycystic ovary syndrome, COVID-19 infection, and vaccine-induced thrombocytopenia and thrombosis and vaccine-induced thrombocytopenia and thrombosis–like disorders. Management centers around anticoagulation, management of the underlying cause, and consideration of invasive measures including endovascular thrombolysis and/or thrombectomy and craniectomy for severe cases. This review discusses the emerging risk factors and their identification, evidence for treatment including the use of direct oral anticoagulants, and the role of invasive management options.

KEYWORDS
cerebral venous sinus thrombosis, estrogen, polycystic ovary syndrome, vaccine-induced thrombocytopenia and thrombosis, venous thromboembolism

1 | INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is an uncommon site of venous thromboembolism (VTE). Previously reported incidence rates range from 1.3 to 2.6 per 100 000 [1–4]. In contrast to other sites of VTE, especially deep vein thrombosis (DVT) and pulmonary embolism (PE), which are more common in men and older age, CVST is more common in younger people and women. In the past, emphasis has been placed on the use of combined oral contraceptives (COCs), thrombophilia, and unusual hematologic disorders as risk factors for CVST. New and emerging risk factors and causes have now been established, including high body mass index (BMI), COVID-19, vaccine-induced thrombocytopenia and thrombosis (VITT), spontaneous VITT, and polycystic ovary syndrome (PCOS). Additionally, until recently, the recommendation was for treatment with a vitamin K antagonist (VKA) rather than a direct oral anticoagulant (DOAC) due to a lack of evidence, and recommendations on duration of anticoagulation were conflicting. Here, we review the contemporary risk factors and etiologies for CVST as well as discuss evidence for the use of DOACs in the treatment of CVST.

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2 | EPIDEMIOLOGY

Prior to the COVID-19 pandemic, population-based studies had estimated the incidence of CVST to be around 15 per million per year [2], and the incidence appeared to be increasing [4]. It was thought that the increasing incidence was mainly due to more sensitive imaging [5]; however, new findings suggest other previously unrecognized forces such as the obesity pandemic may be contributing. It was previously recognized that CVST is more common in women than in men with a ratio of 3:1 and more common in those aged 18 to 44 years [4]. This is in contrast to other forms of VTE that are more common in men, except during women's fertile years, and with increasing incidence with increasing age [6], highlighting the different pathophysiological mechanisms and contributing risk factors at play.

3 | RISK FACTORS

The skewed sex ratio and age at presentation of CVST strongly suggest that the occurrence of CVST is largely driven by female hormonal risk factors—pregnancy and the puerperium, the use of COCs, and PCOS. Both exogenous and endogenous estrogen are known to increase the risk of thrombosis due to a variety of effects on hemostasis, causing elevated levels of von Willebrand factor, factor (F)II, FVII, FVIII, and fibrinogen; reduced levels of tissue factor pathway inhibitor and increased thrombin-activatable fibrinolysis inhibitor; reduced plasma concentrations of antithrombin and protein S; and an acquired resistance to protein C [7]. Furthermore, levels of estradiol, sex hormone binding globulin, and free androgen index have been shown to be associated with VTE risk in nonpregnant women who do not use COCs, indicating a role for endogenous sex hormones in the pathophysiology of VTE in young women [8].

3.1 | Obesity

Obesity is a well-established risk factor for DVT and PE, and it is a recognized major global health problem with increasing incidence. Since 1990, worldwide adult obesity has more than doubled, and in adolescents, it has quadrupled [9]. In 2022, 43% of adults worldwide were overweight and 16% were obese (BMI, ≥30) [9]. In some countries, this rate is even higher, with over 63% of adults in the United Kingdom being overweight or obese [10]. The reasons for the increased risk of VTE stem partly from the fact that adipocytes are very metabolically active cells [11], for adipocytes are able to generate cytokines and adipokines influence coagulation, fibrinolysis, platelet function, and inflammatory responses. Of particular note is that adipocytes produce plasminogen activator inhibitor-1, and leptin, a hormone released from adipocytes, correlates with FVIIa and von Willebrand factor [11,12]. Additionally, obesity is associated with increased activation of platelets [11], activated protein C resistance, and higher concentrations of fibrinogen and FVIII [13]. However, until recently, it was not known if obesity increased the risk of CVST. A case-control study carried out in the Netherlands and Switzerland comprising 186 cases and 6134 controls found that those who were obese had an increased risk of CVST with an odds ratio (OR) of 2.63 (95% CI, 1.53-4.54) [14]. Furthermore, obese women receiving COCs had an increased risk of CVST depending on the degree of weight increase (for BMI of 25-29.9: OR, 11.87; 95% CI, 5.94-23.74; for BMI of ≥30: OR, 29.26; 95% CI, 13.47-63.6) [14]. Specific to CVST, there was speculation that obesity may reduce outflow from the cerebral venous system possibly due to transmittance of increased intra-abdominal pressure; however, whether this explains the increased risk of CVST in obesity is unknown [15].

3.2 | Pregnancy

Pregnancy increases the risk of VTE 5 to 6 times compared with age-matched controls [16]. Family history, presence of inherited thrombophilia, and other medical and pregnancy-related factors further increase this risk. A multicenter case-control study of 163 cases and 1230 controls found pregnant or postpartum women have a 3.5 times higher risk of CVST than nonpregnant or postpartum women of a similar age, most of which was accounted for in the postpartum period [17]. A study of 240 women with cerebrovascular complications during pregnancy found that most women with CVST during pregnancy had a good outcome [18]. A newly recognized contributor to CVST in pregnancy and postpartum is the association of CVST following neuraxial blockade, particularly with accidental dural puncture [19,20]. While limited to case reports and case series resulting in an unknown risk, 1 retrospective single-center study assessing all patients with CVST who presented to their institution found that 19.6% of those with CVST had had a recent dural puncture before the onset of symptoms, either spinal anesthesia or intrathecal chemotherapy [20]. Further studies are needed.

3.3 | COCs

COC medications are among the most frequently prescribed drugs to young women, with an estimated 150 million women using them worldwide [21]. They are well-established as a risk factor for thrombosis, with an increased risk of 2- to 9-fold compared with nonusers in various studies [22]. The risk of VTE is modulated by estrogen dose, type of progestogen, and method of delivery [22,23]. Epidemiologic studies over many years have shown that there is a decreased risk of venous thrombosis with a lower oral estrogen dose—early COCs contained 150 μg ethinyl estrogen, whereas modern formulations contain doses of 20 to 50 μg [22]. Importantly, a large population-based study in Denmark observed that a reduction in oral estrogen dose from 50 μg to 30 to 40 μg daily reduced the risk by 17% to 32%, and a reduction from 30 to 40 μg to 20 μg reduced the risk by 18%, depending on the type of progestogen [24]. The risk also decreases with increasing duration of use (rate ratio compared with nonusers: <1 year, 4.17; 1-4 years, 2.98; and >4 years, 2.76) [24]. Progestins are

formulated in terms of "generations"—first and second generations include levonorgestrel, norethisterone, and medroxyprogesterone; the third generation includes desogestrel, gestodene, and norgestimate; and the fourth generation includes drospirenone [22]. In terms of the type of progestogen, a population-based case-control study in the Netherlands found, relative to nonusers, that the use of COCs containing levonorgestrel was associated with a 4-fold increased risk, 5.6-fold for gestodene, 7.3-fold for desogestrel, 6.8-fold for cyproterone and 6.3-fold for drospirenone [25]. They increase the risk of VTE through various hemostatic mechanisms—increasing levels of FII, FVII, FVIII, and fibrinogen, decreasing antithrombin and protein S levels, and generating an acquired activated protein C resistance [26].

In particular, the risk of CVST increases 5- to 22-fold in those who use COCs [27], and the risk is further increased if the individual has a thrombophilia [28]. A recent systematic review and meta-analysis found that the odds of CVST in women of reproductive age exposed to COCs was 7.59-fold (95% CI, 3.82-15.09) higher than in those not taking COCs [28].

3.4 | PCOS

PCOS is an emerging risk factor for VTE [29]. PCOS is one of the most common endocrine and reproductive disorders thought to affect up to 20% of women worldwide [30,31]. It is a syndrome with a heterogeneous clinical presentation, characterized by an irregular menstrual cycle, ovulatory dysfunction, biochemical and clinical evidence of hyperandrogenism, and polycystic ovary morphology on ultrasound, and is associated with metabolic changes that increase the risk of cardiovascular disease [32]. PCOS may increase the risk of VTE through a number of mechanisms—women with PCOS have been shown to have prothrombotic coagulation changes; they also may be overweight, and many are treated with COCs, which may further modulate risk [29]. The hemostatic changes of PCOS include reduced prothrombin time, activated partial thromboplastin time, and elevated plasminogen activator inhibitor-1 and thrombin-activatable fibrinolysis inhibitor levels [33–35]. Additionally, case-control studies have shown women with PCOS to have greater endogenous thrombin potential and thrombin peak compared with those without PCOS [36], which increases with increasing BMI and insulin resistance [37].

A recent systematic review found that women with PCOS have a 1.5 to 2 times greater risk of VTE than women without PCOS and that this increased risk was not completely explained by excess weight and greater use of COCs in women with PCOS, suggesting that PCOS is an independent risk factor for VTE [29]. The authors of this systematic review conclude that PCOS should be viewed as a risk factor similar to high BMI, age >35 years, or active smoking, particularly when deciding if a COC should be used and at what dose [29], with the suggestion that the least thrombogenic COC be used—low estrogen dose and with levonorgestrel or norgestimate. In terms of PCOS increasing the risk of CVST specifically, there have been case reports [38–40], and further research is required to elucidate if PCOS increases the risk of CVST specifically and through which mechanisms.

3.5 | COVID-19 and other infections

Infections, particularly of the upper respiratory tract and central nervous system, are rare but well-recognized precedents of CVST. Additionally, COVID-19 pneumonia is known to be associated with significant risk of arterial and venous thrombosis, probably related to an increase in proinflammatory cytokines, activation of endothelial cells and platelets, and subsequent activation of coagulation [41]. A retrospective cohort study from the United States in 2020 (before vaccination) found a CVST incident rate among COVID-19–positive inpatients to be 231 per 100 000 person-years [42]. In fact, while much attention was paid to CVST associated with COVID-19 vaccinations (see below), a study actually found that the risk of CVST following COVID-19 infection is 2.3 times higher than following a COVID-19 vaccination [43].

CVST used to be a frequent complication of middle ear and mastoid infections in the preantibiotic era, which became rare with the availability of potent antibiotics [44]. However, cases are still being seen, particularly in the setting of antibiotic resistance. There can be direct spread of the inflammatory process from the middle ear via venules draining into the sigmoid sinuses [44]. Lemierre syndrome, first described in 1936, is a septic thrombophlebitis of the tonsillar and peritonsillar veins secondary to pharyngotonsillitis, which can spread to the internal jugular veins; it similarly had a sharp reduction in incidence with the advent of antibiotics, however, is still seen rarely [45].

3.6 | VITT

VITT is a syndrome characterized by thrombocytopenia, thrombosis, a markedly raised D-dimer, reduced levels of fibrinogen, and the presence of anti–platelet factor-4 (PF4) antibodies following COVID-19 adenovirus vector vaccination [46,47]. It was recognized early on that there were pathogenic similarities with heparin-induced thrombocytopenia (HIT), although the occurrence of VITT is heparin-independent [46]. Of significant importance, enzyme-linked immunosorbent assays (ELISAs) rather than rapid tests are required to detect the anti-PF4 antibodies. Further studies have shown that HIT and VITT antibodies bind to different epitopes on PF4 [48]: HIT antibodies bind to heparin-dependent antigen sites, whereas VITT antibodies bind to different sites on the PF4 molecule [49]. A key characteristic of VITT is the predilection for unusual sites of thrombosis, including the cerebral venous sinuses; indeed, 50% of patients with VITT present with CVST [46]. CVST is usually severe, with thrombosis often involving most major veins and with thrombi extending into the venules, and over one-third can be complicated by secondary intracranial hemorrhage, more common in those with lower platelet counts [46]. Patients with VITT-related CVST also have a much higher mortality rate than those with non-VITT CVST; a registry study of 116 patients with VITT CVST found a mortality rate of 47% (95% CI, 37%-58%) compared with 5% (95% CI, 1%-18%) in those with non-VITT but

TABLE New/emerging risk factors for cerebral venous sinus thrombosis and possible hemostatic pathogenesis.

Risk factor	Risk estimate	Possible hemostatic pathogenesis
Obesity	Odds ratio, 2.63 [14]	Adipocytes release PAI-1; increased fibrinogen, FVIIa, and VWF levels; activated protein C resistance
PCOS	1.5-2× higher risk of VTE [29]	Elevated PAI-1 and TAFI levels. Association with obesity and COC use
COVID-19 infection	Incidence 231 per 100 000 (vs baseline CVST 15 per million) [42]	Increase in proinflammatory cytokines, activation of endothelial cells, and platelets
VITT and VITT-like disorders	Unknown	Platelet activation via production of anti-PF4 antibodies

COC, combined oral contraceptive; CVST, cerebral venous sinus thrombosis; FVIIa, factor VIIa; PAI-1, plasminogen activator inhibitor-1; PCOS, polycystic ovary syndrome; PF4, platelet factor-4; TAFI, thrombin-activatable fibrinolysis inhibitor; VITT, vaccine-induced thrombocytopenia and thrombosis; VTE, venous thromboembolism; VWF, von Willebrand factor.

postadenovirus vaccination CVST and 3.9% (95% CI, 2-7%.4%) in 207 control patients with CVST before the COVID-19 pandemic [50].

More recently, case reports of "VITT-like disorder," also known as "spontaneous VITT," whereby patients have presented with all the signs, symptoms, and hemostatic changes of VITT but without recent vaccination, have been published [51]. Warkentin et al. [52] identified 9 patients with clinical features consistent with a VITT-like disorder, of which 4 presented with CVST. All had moderate to severe thrombocytopenia, very high D-dimer levels, strongly positive anti-PF4 immunoassays by ELISA but not by the chemiluminescent assays (such as HemosIL AcuStar HIT-IgG), and without proximate heparin exposure or adenovirus-based vaccination [52]. A further report of 2 patients with a VITT-like syndrome after adenoviral infection found both of whom had marked thrombocytopenia, very high D-dimer and VITT-like antibodies, and one of these had fatal CVST [53]. Identifying these patients is challenging, and the correct anti-PF4 assay needs to be chosen—rapid HIT assays and functional tests of heparin-induced platelet activation will be negative, and anti-PF4/heparin ELISA tests or modified functional tests (ie, replacement of heparin with PF4) are helpful [52]. The identification of these rare cases is important as not only can it be rapidly life-threatening but treatment with nonheparin anticoagulation and the use of high-dose intravenous immunoglobulin (IVIg) ± plasma exchange for severe cases is also likely to markedly reduce mortality as it has been shown in VITT [46]. We need to learn more about this emerging cause of sudden severe thromboses affecting multiple vascular beds associated with thrombocytopenia and, in particular, the incidence and precipitating factors.

3.7 | Other risk factors

Other well-described contributors to CVST include severe thrombophilias [54], antiphospholipid syndrome, hematologic disorders including myeloproliferative neoplasms and paroxysmal nocturnal hemoglobinuria, malignancy, trauma, certain medications (such as asparaginase) [55], and systemic diseases such as inflammatory bowel disease, thyroid disease, and sarcoidosis, although some of these associations are limited to case reports. Additionally, there are case reports of CVST being associated with episodes of diabetic ketoacidosis and hyperglycemic hyperosmolar state [56,57]. In children and adolescents, there are case reports of individuals with both CVST and iron deficiency anemia [58,59]. However, iron deficiency anemia is common in both women and children, and there are as yet no epidemiological studies to suggest this is a firm relationship; such studies would be welcomed. In 2004, it was noted that approximately 15% of CVST were described as idiopathic; however, this is likely lower now with improved recognition of causes and risk factors [60]. See the Table for the possible hemostatic pathogenesis of the new risk factors.

4 | CLINICAL PRESENTATION

Most cases present with severe headache, but additional signs and symptoms can include seizures, neurological deficits, papilledema, and mental status changes [5]. Approximately 30% to 40% of patients with CVST present with intracranial hemorrhage [61,62]. Clinical findings in CVST are related to (1) increased intracranial pressure (ICP) due to impaired venous drainage and/or (2) focal brain injury from venous ischemia or hemorrhage [63]. Compared with other cerebrovascular diseases, seizures are fairly frequent (in around 40%), bilateral signs may be present, and patients often present with slowly progressive symptoms [63,64]. As noted previously, CVST in VITT often presents with very extensive thrombosis.

5 | WORKUP AND MANAGEMENT

The diagnosis of CVST is based upon clinical suspicion and imaging confirmation. All patients with suspected or confirmed CVST should have a full blood count, renal and liver function, D-dimer, and baseline coagulation tests (prothrombin time, activated partial thromboplastin time, and fibrinogen). Those with features suggestive of VITT (thrombocytopenia and very high D-dimer) should have appropriate testing for VITT antibodies. Importantly, in most cases, early testing for thrombophilia is not helpful, particularly in the case of physiological anticoagulant deficiencies, as acute thrombosis can cause falsely low results. Additionally, in most cases, these results will not

change initial management. The only caveats may be testing for antiphospholipid antibodies or antithrombin deficiency in appropriate clinical scenarios as these results may alter the choice of anticoagulation.

5.1 | Imaging

Computed tomography (CT) is often used as the initial neuroimaging test in patients presenting with new neurological symptoms. Non-contrast CT is often normal in CVST, only demonstrating abnormalities in around 30% of cases, usually hyperdensity of a cortical vein or dural sinus [27]. An ischemic lesion that crosses usual arterial boundaries or is in close proximity to a venous sinus is also suggestive of CVST [65]. Furthermore, those with cortical hemorrhage of unclear origin should also go on to have imaging of the cerebral venous system [66]. Therefore, a high index of suspicion is required to go on to further imaging such as CT venography. Magnetic resonance imaging is more sensitive for the detection of CVST but is less often used in the acute setting due to lack of availability of scanners [63]. A recent scientific statement from the American Heart Association provides an update on diagnosis and management of CVST and states, "MRI/MRV is the recommended non-invasive study of the cerebral venous system to confirm the diagnosis. CT/CTV is a reasonable alternative in centers with limited resources or if the pretest probability is low" [67].

5.2 | Anticoagulation

Once the diagnosis is confirmed, the mainstay of management is anticoagulation. Small studies have demonstrated the safety and efficacy of anticoagulation in this setting. A meta-analysis of 2 randomized trials, with a total of 79 patients, showed that anticoagulation with heparin (unfractionated heparin [UFH] or low-molecular-weight heparin [LMWH]) was associated with a reduction in poor outcomes compared with placebo but it did not reach statistical significance—relative risk of 0.46 (95% CI, 0.16-1.31) for dependency and 0.33 (95% CI, 0.08-1.21) for death [68]. The recommendation to start anticoagulation includes patients with intracerebral hemorrhage at baseline, as the driver for the hemorrhage is high venous pressure [69]. One study directly compared LMWH with UFH in the treatment of 66 adult patients with CVST; 19% of those who received UFH died compared with 0% of those who received LMWH, and this was statistically significant, $P = .01$ [70]. There were 3 patients who had extracranial hemorrhagic complications, all of whom had received UFH, although this was not a prespecified trial outcome. While there were methodological concerns with this study including the fact that the patients allocated to UFH had a more severe baseline condition, the results mirror a Cochrane meta-analysis showing those with DVT and PE treated with LMWH had significantly lower mortality and lower bleeding complications compared with UFH [71].

If VITT or spontaneous VITT is suspected or confirmed, treatment should be aimed at switching off pathological antibodies with the use of IVIg and/or plasma exchange [46]. In these patients, due to similarities with HIT and potential theoretical overlap of reactivity, use of nonheparin anticoagulants, such as argatroban, bivalirudin, or fondaparinux, has been suggested.

5.3 | Endovascular therapies

Endovascular therapies may be considered in patients who fail to improve or clinically deteriorate despite treatment or have signs of raised ICP. These include catheter-directed thrombolysis or thrombectomy. A multicenter randomized trial of 67 patients found that thrombolysis did not result in superior outcomes to anticoagulation alone [72]. A small prospective case series of 20 patients found that while thrombolysis may be effective in severe cases, patients with large infarcts and impending herniation did not benefit [73]. A systematic review of 17 studies involving 235 very high-risk patients treated with endovascular mechanical thrombectomy, which was combined with thrombolysis in most (88%) patients, found that complete radiographic resolution occurred in 69% of patients, although there was no comparator group [74]. They concluded that endovascular thrombectomy was an effective salvage therapy for refractory CVST [74]. Larger studies and meta-analyses have shown that endovascular therapies are associated with higher mortality and should be reserved for use as rescue treatment or in patients with contraindications to standard of care [67]. In particular, case series reporting early use of endovascular therapies in severe cases of CVST associated with VITT that resulted in early reduction in ICP seemed to show benefit [46].

5.4 | Decompressive craniectomy

As the main cause of death of CVST is cerebral herniation, decompressive craniectomy should also be considered in cases of severe intracranial hypertension with limited response to less invasive measures, including early clinical signs of raised ICP such as third nerve palsy as well as in those with large venous infarcts and mass effect causing herniation [75]. This is a reminder that patients with acute CVST should be jointly managed by hematologists and neurologists with access to neurosurgeons, especially those with extensive thrombosis. The 2024 American Heart Association scientific statement on the management of CVST has a new recommendation: "Despite the low level of evidence, decompressive surgery is a life-saving procedure that may result in improved functional outcomes among patients with advanced clinical signs of herniation." [67]. The results of the recently published DECOMPRESS2 (Decompressive Surgery for Patients With Cerebral Venous Thrombosis, Part 2) study, a prospective international cohort study, support this recommendation: of 118 included patients with severe CVST, who had 115 craniectomies and 37 hematoma evacuations, two-thirds were alive and more than one-third independent at 1-year following study [76].

5.5 | Long-term management and choice of anticoagulant

Longer term, the mainstay of management is anticoagulation. Decades-old guidelines suggest anticoagulation for 3 to 6 months in provoked CVST and 6 to 12 months in unprovoked [63]. We believe strongly that in 2024, with the availability of DOACs, consideration for lifelong anticoagulation should be given to those with unprovoked and/or recurrent CVST and those with an ongoing risk factor or with a high-risk thrombophilia such as antiphospholipid syndrome or antithrombin deficiency. A retrospective study found that CVST recurrence occurred in 4.4% of 706 patients after anticoagulation withdrawal, with a median follow-up of 40 months [77]. Most recurrences occur within the first year. Risk factors for recurrence included history of VTE, male sex, polycythemia, and/or thrombocytosis [78]. It is interesting that recurrence rates after CVST are lower than other forms of VTE, whereby long-term anticoagulation is now generally recommended after first unprovoked VTE [79]. This again highlights that CVST has a distinct pathophysiology and clinical course.

Traditionally, VKAs have been the anticoagulant of choice. Recent evidence suggests DOACs are safe and effective in the treatment of CVST, although further prospective studies are required. A systematic review from 2021 found only 1 randomized controlled trial, as well as 5 observational studies and 27 case series with a total of 279 patients, and reported a similar risk of death in DOAC vs standard therapy arms (relative risk [RR] , 2.12; 95% CI, 0.29-15.59) [80]. The RE-SPECT CVT (A Clinical Trial Comparing Efficacy and Safety of Dabigatran Etexilate With Warfarin in Patients With Cerebral Venous and Dural Sinus Thrombosis) trial comparing dabigatran with VKA found no recurrent thrombosis in either group with higher rates of bleeding in those receiving VKA [81]. Another meta-analysis included 1735 patients in observational studies and 215 in randomized trials and found DOACs had comparable risk of recurrent VTE (RR, 0.85; 95% CI, 0.52-1.37), major hemorrhage (RR, 0.70; 95% CI, 0.4-1.21), intracranial hemorrhage (RR, 0.58; 95% CI, 0.3-1.12), death (RR, 1.14; 95% CI, 0.54-2.43), and compete venous recanalization (RR, 0.98; 95% CI, 0.87-1.11) compared with VKAs [82]. We eagerly await the results of the DOAC-CVT (Direct Oral Anticoagulants for the Treatment of Cerebral Venous Thrombosis) trial, an international, prospective, observational cohort study comparing DOACs with VKA aiming to recruit 500 patients (ClinicalTrials.gov identifier, NCT04660747) [83]. VKA and LMWH still have a place in those with triple-positive antiphospholipid syndrome and pregnancy, respectively.

6 | CONCLUSION

CVST is a rare but serious form of VTE that has distinct pathophysiology, risk factors, and clinical course to other forms of VTE. In particular, it more commonly affects fertile women. Assessment should include consideration of BMI, questioning the use of COCs, presence of PCOS, and the potential for spontaneous VITT alongside more traditional risk factors.

Treatment is centered around anticoagulation, with special treatments of IVIg and/or plasma exchange for those with confirmed or suspected VITT. Finally, limited data suggest that DOACs seem to be safe and effective in those with CVST who are not pregnant or breastfeeding.

AUTHOR CONTRIBUTIONS

B.J.H. conceived the study, and B.J.H. and C.D. reviewed and interpreted the literature and wrote and reviewed the manuscript.

DECLARATION OF COMPETING INTERESTS

There are no competing interests to disclose.

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