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CEREBRAL VENOUS THROMBOSIS: AN OVERVIEW OF CLINICAL FEATURES, DIAGNOSIS, AND TREATMENT

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ABSTRACT

This narrative review synthesizes current evidence from 2016-2025 articles on cerebral venous thrombosis (CVT), a rare cerebrovascular condition accounting for 0.5-1% of all strokes that predominantly affects young adults, particularly women (3:1 ratio) due to hormonal risk factors. The COVID-19 pandemic introduced novel dimensions including SARS-CoV-2-associated CVT (0.08% incidence) and vaccine-induced immune thrombotic thrombocytopenia (VITT) requiring specific management protocols. Clinical presentation remains heterogeneous, with headache occurring in 60-95% of cases, though 6-25% present with isolated headache without focal signs, necessitating high clinical suspicion and advanced neuroimaging (MRI/MRV as gold standard) for diagnosis. Anticoagulation represents the treatment cornerstone, with accumulating evidence from randomized trials (RE-SPECT CVT, ACTION-CVT, EINSTEIN-Jr CVT) demonstrating that direct oral anticoagulants offer safe and effective alternatives to warfarin, though optimal duration remains debated. Contemporary management has dramatically improved prognosis, reducing mortality from historical 30-50% to current 5-10%, with approximately 80% of patients achieving functional independence, with recurrence risk of ~4% annually and substantial minorities suffer persistent headache, cognitive difficulties, or seizures. Future research priorities include defining optimal anticoagulation duration, standardizing endovascular intervention protocols, and identifying biomarkers for early diagnosis and prognostic stratification.

KEYWORDS

Cerebral Venous Thrombosis, Cerebral Venous Sinus Thrombosis, Stroke in Young Adults, Anticoagulation, Direct Oral Anticoagulants

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Introduction

Cerebral venous thrombosis (CVT), known also as cerebral venous sinus thrombosis (CVST), represents a rare and often underdiagnosed form of cerebrovascular disease. The basis of the disease is partial or complete thrombotic occlusion of the cerebral veins or dural sinuses (Moraes Junior & Conforto, 2022). While sharing the broader category of stroke with arterial ischemic events, CVT differs fundamentally in its pathophysiology, epidemiology, clinical presentation, diagnostic approach, and therapeutic management (Dmytriw et al., 2018). Clinical presentation is remarkably heterogeneous. Symptoms may develop acutely, subacutely, or chronically (Dmytriw et al., 2018), which significantly complicates the diagnostic process. While arterial ischemic stroke most frequently affects elderly individuals with accumulated vascular risk factors, with increasing incidence with advancing age, CVT exhibits a marked predilection for younger populations (Silvis et al., 2017; Hou et al., 2024). This demographic distribution carries profound societal and economic implications, as CVT frequently affects individuals during peak years of professional productivity, family formation, and parenting responsibilities (Ferro & Aguiar de Sousa, 2019).

Methodology

This narrative review was conducted to synthesize and analyze current evidence on cerebral venous thrombosis, focusing on clinical features, diagnostic approaches, and treatment strategies. The source material for this review consisted of 32 scientific articles. These articles included original research studies, systematic reviews and meta-analyses, clinical trials, expert consensus guidelines, and review articles published between 2016 and 2025. Each article was thoroughly reviewed to extract relevant information pertaining to the objectives of this narrative review. While conducting a narrative review, particular attention was paid to the quality and level of evidence provided by each source.

Results

1. Epidemiology

CVT accounts for approximately 0.5-1% of all stroke cases globally (Moraes Junior & Conforto, 2022; Idiculla et al., 2020). However, these figures likely underestimate the true prevalence due to underdiagnosis and misdiagnosis, particularly in resource-limited settings. Notably, CVT demonstrates a striking gender disparity, with women affected three times more frequently than men, primarily attributable to sex specific risk factors specific that including pregnancy, puerperium, and use of oral contraceptives (Silvis et al., 2017; Aguiar de Sousa et al., 2021). Large studies, like the VENOST Study encompassing 1144 patients from over 35 hospitals, have substantially enhanced our understanding of CVT epidemiology over the past two decades (Duman et al., 2017). Geographic variations in incidence and risk factor profiles have been documented, with higher rates reported in developing countries, potentially reflecting differences in genetic predisposition, healthcare access, and prevalence of risk factor (Duman et al., 2017).

2. Risk Factors

The spectrum of risk factors CVT is broad and heterogeneous, encompassing genetic predispositions, acquired prothrombotic states, hormonal influences, inflammatory conditions, and local mechanical factors. In the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT), at least one identifiable risk factor was found in the vast majority of patients, underscoring the multifactorial etiology of CVT (Ferro et al., 2017). Understanding these risk factors is essential for the diagnosis process, risk stratification, and implementing prevention strategies.

Gender-specific risk factors account for a substantial proportion of CVT cases, particularly in women of childbearing age. Use of oral contraceptives is one of the most significant and modifiable risk factors, conferring a risk of 7,6-fold compared to non-users (Ferro et al., 2017). Zuurbier and Coutinho (2016) reported that more than 50% of women with CVT were using oral contraceptives at the time of diagnosis. That highlight the importance of this risk factor in clinical practice.Pregnancy and the puerperium constitute another critical category of risk factors, with the puerperium representing a particularly high-risk period (Ferro & Aguiar de Sousa, 2019). The risk is highest during the first months following delivery which could be related to physiological changes in activity of coagulation factors and mechanical factors such as venous stasis. (Ferro & Aguiar de Sousa, 2019).

Other epidemiological studies have identified obesity as an independent risk factor for CVT, also previously underrecognized anemia has emerged as potential (Ferro & Aguiar de Sousa, 2019).

Inherited thrombophilias represent an important category of genetic predispositions to CVT, though their precise contribution remains a subject of ongoing investigation. Authors discuss various hereditary thrombophilic conditions as risk factors of CVT, including factor V Leiden mutation, prothrombin G20210A mutation, and deficiencies of anticoagulants: protein C, protein S, and antithrombin. (Ferro et al., 2017) However, specific prevalence estimates for these conditions within CVT populations require careful interpretation, as the cited literature does not always provide precise quantitative data. Among acquired thrombophilias, antiphospholipid syndrome (APS) holds particular clinical significance. Silvis et al. (2017) reported that antiphospholipid syndrome was identified in 6-17% of CVT patients, representing a broader range than commonly cited. Importantly, the presence of APS may have implications for recurrence risk and long-term anticoagulation decisions, though the specific relationship between APS and CVT recurrence warrants further investigation through prospective studies.

Infections, both local and systemic, have long been recognized as precipitants of CVT, though their relative contribution has decreased in the modern antibiotic era. Local infections affecting the head and neck region—including otitis media, mastoiditis, sinusitis, and dental infections—can lead to septic thrombophlebitis through direct extension or hematogenous spread. (Idiculla et al., 2020, Ferro et al., 2017, Almegren, 2025) Also systemic infections like HIV, tuberculosis, and sepsis are considered a risk factor. (Idiculla et al., 2020). The available data suggest varying prevalence rates, authors citing data from large international studies, reported infection rates of approximately 7% in CVT cohorts, though prevalence varies significantly across different populations and healthcare settings. (Idiculla et al., 2020)

Autoimmune and inflammatory diseases also constitute an important category of risk factors. The authors mention association with conditions including Behçet's disease, systemic lupus erythematosus (SLE), antiphospholipid syndrome, and Sjögren's syndrome (Zhang et al., 2021).

Malignancies also represent risk factors for CVT. Authors reported that malignancy was identified in approximately 7.4% of CVT cases.(Ranjan et al., 2023). Both primary brain tumors and systemic malignancies have been implicated in CVT pathogenesis (Idiculla et al., 2020). Hematological malignancies appear particularly important according to venous thrombotic complications (Zuurbier & Coutinho, 2016).

Beyond the major risk factors discussed above, numerous other conditions and circumstances have been associated with CVT. Mechanical factors such as head trauma and neurosurgical procedures including craniotomy and placement of indwelling ventricular catheters have been identified as risk factors (Spadaro et al., 2021). Also dehydration has been identified as a rare contributing factor in some CVT cases (Duman et al., 2017).

The recent COVID-19 pandemic has introduced a new dimension to CVT epidemiology, with both SARS-CoV-2 infection itself, through mechanisms including cytokine storm, direct immune-mediated processes, and endothelial damage (Baldini et al., 2021) and certain COVID-19 vaccines (particularly adenovirus-vector vaccines) associated with CVT through distinct mechanisms involving vaccine-induced immune thrombotic thrombocytopenia (VITT) (Baldini et al., 2021; Moraes Junior & Conforto, 2022).

Importantly, despite comprehensive evaluation, a part of CVT cases remain idiopathic, with no identifiable risk factor (Aguiar de Sousa, 2021; Ulivi et al., 2020). This observation suggests that additional genetic, environmental, or multifactorial determinants remain to be elucidated.

Table 1. Risk Factors for Cerebral Venous Thrombosis

Category	Risk Factor
HORMONAL / GENDER-SPECIFIC	Oral contraceptives
	Pregnancy & puerperium
METABOLIC	Obesity
	Anemia
GENETIC / INHERITED THROMBOPHILIAS	Factor V Leiden mutation
	Prothrombin G20210A mutation
	Protein C deficiency
	Protein S deficiency
	Antithrombin deficiency
ACQUIRED THROMBOPHILIAS	Antiphospholipid syndrome (APS)
INFECTIONS	Local infections
	Systemic infections
AUTOIMMUNE / INFLAMMATORY	Behçet's disease
	Systemic lupus erythematosus (SLE)
	Sjögren's syndrome
MALIGNANCY	Malignancies (local and systemic)
MECHANICAL	Head trauma
	Neurosurgical procedures
OTHER	Dehydration
COVID-19 RELATED	SARS-CoV-2 infection
	COVID-19 vaccines (adenovirus-vector)
IDIOPATHIC	No identifiable risk factor

3. Pathophysiology

The pathophysiology of CVT differs fundamentally from that of arterial stroke, involving complex mechanisms that lead to venous congestion, impaired cerebrospinal fluid absorption, and parenchymal injury. Understanding these mechanisms is essential for comprehending the clinical manifestations and guiding therapeutic decisions.

Normal cerebral venous drainage occurs through a network of superficial and deep cerebral veins that empty into dural venous sinuses, which ultimately drain into the internal jugular veins (Jianu et al., 2022).The dural sinuses most commonly affected by thrombosis are the superior sagittal sinus (approximately 70% of cases) and the transverse/sigmoid sinuses, which are frequently involved together, with multiple sinuses affected simultaneously in over 70-90% of patients (Almegren, 2025; Dmytriw et al., 2018).

When thrombosis occludes cerebral veins or sinuses, several pathophysiological consequences ensue. First, venous outflow obstruction leads to increased venous pressure in the affected territory, resulting in venous congestion and reduced cerebral perfusion (Jianu et al., 2022). This venous hypertension increases capillary hydrostatic pressure, leading to disruption of the blood-brain barrier and vasogenic edema (Jianu et al., 2022).If venous pressure exceeds a critical threshold and compensatory collateral drainage is insufficient, capillary rupture occurs, resulting in hemorrhagic transformation—a feature of CVT observed in a substantial proportion of cases (Zuurbier & Coutinho, 2016). Second, impaired absorption of cerebrospinal fluid (CSF) at the arachnoid granulations, which project into the dural sinuses, results in elevated intracranial pressure (Almegren, 2025; Silvis et al., 2017). This mechanism explains the syndrome of isolated intracranial hypertension that occurs in a subset of CVT patients, characterized by headache and papilledema without focal neurological deficits or parenchymal lesions (Idiculla et al., 2020). The elevated intracranial pressure may lead to decreased cerebral perfusion pressure through its effects on the pressure gradient driving cerebral blood flow. Third, in severe cases with extensive venous occlusion or inadequate collateral compensation, ischemia and cytotoxic edema develop, leading to venous infarction (Jianu et al., 2022; Aguiar de Sousa, 2021). Venous infarctions differ from arterial infarctions in several respects: they do not conform to arterial territories, frequently demonstrate hemorrhagic transformation, and show variable patterns of diffusion restriction on MRI reflecting the mixed vasogenic and cytotoxic components (Dmytriw et al., 2018). The extent and severity of these pathophysiological processes depend on several factors. The adequacy of collateral venous drainage determines the severity of pathophysiological consequences, with the extensive anastomoses of the cerebral venous system often providing sufficient compensation for venous occlusion (Silvis et al., 2017). The location of thrombosis determines both the venous territory affected and the availability of alternative drainage routes. Individual variation in venous anatomy, including the presence of accessory sinuses and bridging veins, affects vulnerability to venous occlusion (Dmytriw et al., 2018). The thrombotic process itself involves activation of the coagulation cascade triggered by one or more of Virchow's triad components: venous stasis, endothelial injury, and hypercoagulability (Almegren, 2025). Once formed, the thrombus may propagate along the affected vein or sinus, potentially extending to involve additional venous structures. The thrombus may also organize and recanalize over time, a process that occurs in a substantial proportion of patients depending on the location, extent of thrombosis, and timing of follow-up imaging (Aguiar de Sousa et al., 2018). Recanalization typically begins within days to weeks of anticoagulation initiation and is associated with better clinical outcomes, though complete recanalization is not necessary for favorable recovery (Aguiar de Sousa et al., 2018; Rosa et al., 2024).

4. Clinical Presentation

The clinical presentation of CVT is remarkably heterogeneous, often posing diagnostic challenges due to its variable symptoms, diverse syndromes, and temporal evolution that can range from acute to chronic (Silvis et al., 2017). This variability reflects differences in the location, extent, and rapidity of thrombosis, as well as individual variations in collateral venous drainage and compensatory mechanisms.

Headache: The Cardinal Symptom

Headache occurs in a majority of CVT patients, with reported frequencies ranging from 60% to 95% across various studies (Mehta et al., 2019; Almegren, 2025; Idiculla et al., 2020). The ISCVT cohort reported headache in 89% of patients. Approximately 6-25% present with isolated headache without focal signs, creating substantial diagnostic challenges (Mehta et al., 2019; Spadaro et al., 2021). CVT headache characteristics vary considerably. The pain is typically severe, diffuse, and persistent. In rare cases, CVT can present as a thunderclap headache (Mehta et al., 2019). Unlike migraine, CVT headache generally lacks clear triggers, demonstrates persistent rather than episodic character, and exhibits poor response to standard analgesics (Ulivi et al., 2020). One large study found that headache onset was acute (1-3 days) in 60% of patients, subacute (4-14 days) in 24%, and chronic (>14 days) in 10%, with most CVT headaches appearing over a 1-14 day period (Mehta et al., 2019). Red flag features warranting urgent neuroimaging include: sudden-onset severe headache, new or qualitatively different headache, headache with neurological deficits or altered consciousness, headache with papilledema, peripartum headache. (Mehta et al., 2019; Ulivi et al., 2020; Saposnik et al., 2024).

Seizures

Seizures are a common manifestation in CVT patients and represent the presenting manifestation in a substantial subset of cases (Ferro et al., 2017; Gurram et al., 2024). This frequency substantially exceeds that seen in arterial stroke, reflecting fundamental pathophysiological differences (Duman et al., 2017). Seizures may present with various clinical manifestations (Ferro et al., 2017; Duman et al., 2017). Early seizures occur within the first 24 hours in a significant proportion of CVT patients. (Duman et al., 2017). Late seizures can develop in some patients (Ferro et al., 2017)

Focal Neurological Deficits

Focal deficits occur in 30-50% of CVT patients (Silvis et al., 2017; Ranjan & Sharma, 2023). Motor symptoms are most frequent, followed by visual impairment and aphasia, whereas sensory symptoms are less common (Ulivi et al., 2020). Unlike arterial stroke, CVT-related deficits frequently exhibit subacute or gradual evolution over days to weeks rather than sudden onset (Ulivi et al., 2020; Ranjan & Sharma, 2023). Bilateral deficits occur more commonly in CVT due to deep venous system thrombosis with bilateral thalamic involvement (Ulivi et al., 2020; Dmytriw et al., 2018).

Encephalopathy and Altered Mental Status

Altered mental status occurs in 15-25% of CVT patients and represents a powerful predictor of poor outcome (Idiculla et al., 2020; Silvis et al., 2017). Deep cerebral venous system thrombosis characteristically produces profound encephalopathy due to bilateral thalamic and basal ganglia involvement (Dmytriw et al., 2018). Coma at presentation historically carried mortality exceeding 50%. However, contemporary series demonstrate that with aggressive management, approximately one-third of comatose CVT patients can achieve complete functional recovery (Ferro & Aguiar de Sousa, 2019).

Papilledema and Intracranial Hypertension

Papilledema occurs in approximately 28% of CVT patients based on ISCVT data (Idiculla et al., 2020; Ferro et al., 2017). The isolated intracranial hypertension syndrome, characterized by headache and papilledema without focal deficits or parenchymal lesions, occurs in a subset of CVT patients (Idiculla et al., 2020; Rosa et al., 2024). Associated visual symptoms include transient visual obscurations (13-27%), diplopia from sixth nerve palsy (6-14%), and progressive visual field loss (Saposnik et al., 2024). Permanent visual loss can affect survivors when intracranial hypertension remains uncontrolled (Ferro et al., 2017). The isolated intracranial hypertension presentation creates diagnostic challenges due to overlap with idiopathic intracranial hypertension, necessitating neuroimaging with venous phase evaluation in all suspected cases (Saposnik et al., 2024).

Pediatric CVT

Pediatric CVT commonly presents with headache (71%), focal neurological deficits (30%), and seizures (11%), with infection being the most common risk factor (Connor et al., 2020). Diagnosis requires particular vigilance as symptoms may be nonspecific in preverbal children (Connor et al., 2020).

5. Diagnosis

The diagnosis of CVT requires a high index of suspicion given its variable presentation, combined with appropriate neuroimaging to confirm the presence of venous thrombosis and characterize associated parenchymal abnormalities. The diagnostic evaluation encompasses clinical assessment, laboratory investigations, neuroimaging, and occasionally invasive procedures. Clinical suspicion for CVT should be raised in patients presenting with unusual or atypical stroke presentations, particularly in younger patients, those with multiple stroke risk factors, or those with known prothrombotic conditions (Spadaro et al., 2021; Ulivi et al., 2020).

Imaging tests

Neuroimaging represents the cornerstone of CVT diagnosis. While non-contrast computed tomography (CT) is often the initial imaging study in patients presenting with acute neurological symptoms, it has limited sensitivity for detecting CVT, with abnormalities evident in only 30-40% of cases (Dmytriw et al., 2018; Spadaro et al., 2021). Direct signs of thrombosis on non-contrast CT include the “dense triangle sign” (hyperdensity of the superior sagittal sinus) and the “cord sign” (hyperdense cortical vein), which are visible in limitedof cases and primarily during the acute phase when fresh thrombus appears hyperdense (Dmytriw et al., 2018). Indirect signs include cerebral edema, hemorrhagic infarction, or diffuse brain swelling, but these findings are non-specific and may be absent in mild cases (Almegren, 2025). CT venography (CTV) dramatically improves diagnostic sensitivity and specificity and has become a first-line imaging modality in many institutions due to its wide availability, rapid acquisition, and reliability (Ferro et al., 2017; Dmytriw et al., 2018). CTV directly visualizes the cerebral venous anatomy following intravenous contrast administration and demonstrates the “empty delta sign” (filling defect within the sinus representing thrombus surrounded by contrast-enhanced dura) or absent filling of the affected venous structures (Saposnik et al., 2024). CTV is particularly valuable in the emergency setting where rapid diagnosis is needed and MRI access may be limited.

Magnetic resonance imaging (MRI) combined with magnetic resonance venography (MRV) is considered the gold standard for CVT diagnosis, offering superior sensitivity and specificity, better characterization of parenchymal lesions, and the ability to date thrombus age based on signal characteristics (Ferro et al., 2017; Dmytriw et al., 2018; Rosa et al., 2024). On conventional MRI sequences, acute thrombus appears isointense on T1 and hypointense on T2, subacute thrombus becomes hyperintense on both T1 and T2 due to methemoglobin formation, and chronic thrombus shows variable signal intensity (Dmytriw et al., 2018). MRV, typically performed using time-of-flight (TOF) or contrast-enhanced techniques, directly demonstrates absent flow signal in thrombosed venous structures and has excellent sensitivity for major sinus thrombosis (Dmytriw et al., 2018; Rosa et al., 2024). However, MRV may have limitations in detecting isolated cortical vein thrombosis or partial/non-occlusive thrombus, and anatomical variants (such as hypoplastic or absent transverse sinus) can mimic thrombosis, necessitating correlation with conventional sequences to distinguish true thrombosis from flow gaps (Ferro et al., 2017). Recent evidence suggests that contrast-enhanced MRI and susceptibility-weighted imaging offer increased sensitivity for detecting cortical vein thrombosis compared to standard MRV sequences (Rosa et al., 2024). Hemorrhagic infarctions not conforming to arterial territories, or lesions in unusual locations should raise suspicion for CVT (Ulivi et al., 2020; Almegren, 2025).

Catheter angiography, once the diagnostic gold standard, is now rarely required for diagnosis given the high accuracy of non-invasive imaging, but may occasionally be performed when non-invasive studies are inconclusive or when endovascular intervention is being considered (Ferro et al., 2017; Dmytriw et al., 2018).

Laboratory tests

Laboratory evaluation in suspected CVT serves multiple purposes: identifying underlying prothrombotic conditions, evaluating for alternative diagnoses, and assessing disease severity. While no specific blood test confirms CVT, certain findings may support the diagnosis or guide etiological investigation (Ulivi et al., 2020; Saposnik et al., 2024). D-dimer levels are elevated in approximately 80-90% of CVT patients, and normal D-dimer (<500 ng/mL) has good negative predictive value, though its specificity is limited by elevation in many other conditions (Ferro et al., 2017; Spadaro et al., 2021). Importantly, normal D-dimer does not exclude CVT, particularly in patients with isolated intracranial hypertension syndrome or chronic presentations (Ulivi et al., 2020). Thrombophilia screening should be considered in most CVT patients, particularly younger individuals without obvious provoked causes, those with family history of thrombosis, and those with recurrent events. Testing should include factor V Leiden mutation, prothrombin G20210A mutation, protein C and S levels, antithrombin III level, antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, anti-β2-glycoprotein I antibodies), and homocysteine level (Ferro et al., 2017; Ulivi et al., 2020). Timing of thrombophilia testing is important, as acute thrombosis and anticoagulation can affect results; ideally, testing should be performed after the acute phase and off anticoagulation when feasible, or repeated later to confirm abnormalities. Additional laboratory investigations may be indicated based on clinical presentation and risk factor assessment, including: pregnancy testing in women of childbearing age; complete blood count to assess for polycythemia, thrombocytosis, or anemia; HIV and hepatitis serology; erythrocyte sedimentation rate and C-reactive protein for inflammatory conditions; antinuclear antibodies and other autoimmune markers if connective tissue disease is suspected; and protein electrophoresis if hyperviscosity syndrome is considered (Zhang et al., 2021; Ulivi et al., 2020). Cerebrospinal fluid (CSF) examination through lumbar puncture is not routinely required for CVT diagnosis and may be contraindicated in patients with increased intracranial pressure and mass effect (Ferro et al., 2017). However, could be performed to exclude alternative diagnoses such as meningitis or subarachnoid hemorrhage. The American Heart Association scientific statement on CVT diagnosis and management provides diagnostic algorithms emphasizing that CVT should be considered in the differential diagnosis of headache, stroke in young adults, seizures, and encephalopathy, with neuroimaging (CTV or MRI/MRV) performed promptly in suspected cases (Saposnik et al., 2024). For patients presenting to emergency departments with headache and neurological symptoms, a screening non-contrast CT may be performed initially, but if CVT is suspected clinically, dedicated venous imaging (CTV or MRV) should be obtained even if the initial CT appears normal (Spadaro et al., 2021).

6. Treatment Strategies

Anticoagulation Therapy

Anticoagulation represents CVT treatment cornerstone, addressing underlying thrombotic process and preventing thrombus propagation (Ferro et al., 2017; Saposnik et al., 2024). Current guidelines from European Stroke Organization and American Heart Association recommend initiating anticoagulation in all confirmed CVT patients, including those with intracranial hemorrhage, unless specific contraindications exist (Ferro et al., 2017; Saposnik et al., 2024). This recommendation, initially controversial due to hemorrhagic complication concerns, is now well-established based on randomized trials and large observational studies demonstrating safety and efficacy.

Acute-phase anticoagulation typically uses low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH). LMWH is generally preferred for predictable pharmacokinetics, subcutaneous administration, and lack of monitoring requirement, though UFH may be selected in severe renal impairment, anticipated procedures requiring rapid reversal, or critically ill patients (Ferro et al., 2017; Ulivi et al., 2020). Typical LMWH dosing is weight-based and should be adjusted for renal function (Saposnik et al., 2024).

For long-term anticoagulation, vitamin K antagonists (VKAs) like warfarin have traditionally been standard care, targeting INR 2.0-3.0 (Ferro et al., 2017). Major VKA limitations include monitoring requirement, dietary restrictions, drug interactions, and individual dose response variation. Direct oral anticoagulants (DOACs) have transformed the CVT anticoagulation landscape, offering several potential advantages over VKAs including fixed dosing, no monitoring, fewer drug and food interactions, and potentially better safety profiles (Alimohammadi et al., 2022). The RE-SPECT CVT trial represented a landmark study investigating dabigatran (DOAC) versus warfarin (VKA) (Ferro et al., 2019). This international randomized exploratory trial included 120 patients with acute CVT randomized to dabigatran 150mg twice daily versus dose-adjusted warfarin (target INR 2.0-3.0) for 6 months. The primary efficacy outcome was recurrent venous thromboembolism; primary safety outcome was major bleeding. No recurrent VTE events were observed in either group. Major bleeding or venous thrombotic events occurred in 1 patient (1.7%) in the dabigatran group (one intestinal bleeding) versus 2 patients (3.3%) in the warfarin group (two intracranial hemorrhages). Due to the limited sample size and low event rates, the study was not powered to demonstrate non-inferiority or superiority of either treatment. However, the results suggested similar safety and efficacy profiles, with the caveat that definitive conclusions require larger trials. Multiple observational studies support DOAC use. The ACTION-CVT multicenter international study compared DOACs (rivaroxaban, apixaban, dabigatran) versus warfarin in 845 CVT patients who met inclusion criteria from an initial cohort of 1,025 patients (Yaghi et al., 2022). During median follow-up of 345 days, the study found similar rates of recurrent venous thrombosis (5.26 per 100 patient-years for DOACs versus 5.87 per 100 patient-years for warfarin, p=0.61) and significantly lower rates of major hemorrhage with DOACs (adjusted hazard ratio 0.35, 95% CI 0.15-0.82, p=0.02). Recanalization rates were similar between groups. The study supported DOAC safety and efficacy in real-world CVT practice. The EINSTEIN-Jr CVT trial demonstrated rivaroxaban safety and efficacy in pediatric CVT, an important special population (Connor et al., 2020). This open-label, randomized trial included 114 children with confirmed CVT (from 117 initially randomized), comparing rivaroxaban (n=73) to standard anticoagulation (n=41) in a 2:1 ratio. Symptomatic recurrent VTE occurred in 0% of the rivaroxaban group versus 2.4% (1/41) of the standard group. Clinically relevant bleeding was observed in 5 rivaroxaban recipients (6.8%, all nonmajor extracranial events) versus 1 standard anticoagulation recipient (2.4%, one major subdural bleeding event). No major bleeding occurred in the rivaroxaban group. The trial supported rivaroxaban as a reasonable alternative in pediatric CVT. Systematic reviews have synthesized accumulating DOAC evidence. Bose et al. (2021) conducted systematic review of DOACs for CVT treatment, including 33 studies with 279 DOAC-treated patients and 315 receiving standard therapy. The review found no significant differences between DOACs and standard therapy for outcomes including death, recurrent CVT, or incomplete recanalization. The study concluded DOACs appear safe and effective alternatives to VKAs, though noted most evidence was from observational studies. Chen et al. (2024) performed meta-analysis of randomized controlled trials comparing DOACs to standard anticoagulation in CVT. Analysis included 4 RCTs with 270 patients. Pooled results showed DOACs had similar rates of recurrent VTE (0.9% vs 0%, risk difference 1%, 95% CI -3% to 4%, p=0.61) and major bleeding (1.2% vs 2.4%, risk difference -1%, 95% CI -6% to 3%, p=0.61) compared to standard anticoagulation. Both groups demonstrated low incidence rates of these outcomes. The meta-analysis provided evidence supporting DOAC use as an alternative to VKAs.

Based on accumulating evidence, recent guidelines support DOACs as reasonable alternatives to warfarin for CVT anticoagulation (Saposnik et al., 2024). The American Heart Association scientific statement acknowledges DOACs appear to be safe and effective alternative options to VKAs for long-term anticoagulation in CVT patients, though VKAs remain acceptable. DOAC selection should consider patient factors including renal function, drug interactions, adherence capability, and cost. DOACs should be avoided in pregnancy, severe renal impairment (creatinine clearance <30 mL/min), antiphospholipid antibody syndrome, and potentially in high-risk situations like extensive thrombosis with large hemorrhagic infarctions until more data become available. Anticoagulation duration remains a debated area with limited definitive evidence. Current guidelines generally recommend 3 to 12 months of anticoagulation for CVT with transient (provoked) risk factors, and indefinite anticoagulation for persistent or chronic major risk factors, recurrent venous thromboembolism, or severe thrombophilia (Ferro et al., 2017; Saposnik et al., 2024). European Stroke Organization guidelines suggest minimum 3 months for all patients, with extension to 12 months for unprovoked cases or mild thrombophilia, and indefinite duration for severe thrombophilia or recurrent events (Ferro et al., 2017).

Symptomatic and Adjunctive Treatment

Beyond anticoagulation, symptomatic management addresses complications and prevents secondary injury. Seizure management is important given their common occurrence (Duman et al., 2017; Gurram et al., 2024). Acute seizures should be treated promptly with antiepileptic drugs (AEDs). However, prophylactic AED use in seizure-free patients remains controversial. European Stroke Organization guidelines suggest antiepileptic drugs in patients with supratentorial lesions who have had seizures to prevent early recurrent seizures, but prophylactic AEDs in seizure-free patients are not recommended (Ferro et al., 2017) The American Heart Association statement echoes this, recommending AEDs for seizure treatment but not routine prophylaxis (Saposnik et al., 2024). If seizures occur, AEDs are typically used, though the optimal duration of therapy remains unclear and should be individualized based on risk factors and clinical course. General measures for intracranial hypertension include head elevation, avoiding hypotension, osmotic therapy, and hyperventilation (Ulivi et al., 2020). For severe intracranial hypertension, osmotic therapy with mannitol or hypertonic saline may be used, though evidence is limited to case series and extrapolation from other intracranial hypertension causes (Ulivi et al., 2020). Acetazolamide, a carbonic anhydrase inhibitor reducing CSF production, has been used in isolated intracranial hypertension syndrome but lacks robust evidence (Ferro et al., 2017). For isolated intracranial hypertension syndrome with severe papilledema risking vision loss, therapeutic lumbar punctures may provide temporary relief by removing CSF and reducing pressure (Ulivi et al., 2020). Supportive care includes maintaining adequate hydration to avoid hemoconcentration, managing fever which may worsen neurological injury, monitoring for complications, and providing venous thromboembolism prophylaxis for immobilized patients (Saposnik et al., 2024). Rehabilitation services including physical, occupational, and speech therapy should be initiated early for patients with neurological deficits.

Endovascular and Surgical Interventions

For severe CVT with clinical deterioration despite adequate medical therapy, more aggressive interventions may be considered (Coutinho et al., 2020). Proposed endovascular treatment options include mechanical thrombectomy (using aspiration catheters or stent retrievers), catheter-directed thrombolysis, or a combination of techniques, but the evidence for their effectiveness is uncertain, as reflected in the guidelines. American Heart Association statement indicates endovascular therapies are reserved for patients with evidence of thrombus propagation, individuals with neurological deterioration despite medical therapy, or those with contraindications, noting lack of controlled studies and poorer outcomes in meta-analyses (Saposnik et al., 2024).

Decompressive craniectomy represents life-saving intervention for malignant CVT with large space-occupying hemorrhagic infarctions and impending herniation (Moraes Junior & Conforto, 2022). Unlike endovascular therapy, decompressive surgery has more consistent evidence supporting use in selected severe cases. Studies suggest approximately one-third of severe CVT patients undergoing decompressive craniectomy can achieve functional independence (mRS 0-2) one year after surgery (Moraes Junior & Conforto, 2022). The mechanism is similar to decompressive hemicraniectomy for malignant middle cerebral artery infarction, providing space for brain swelling and preventing herniation. Indications for decompressive craniectomy include: clinical deterioration with signs of herniation (pupillary abnormalities, progressive decrease in consciousness, decerebrate posturing); large unilateral or bilateral space-occupying hemorrhagic infarctions; significant midline shift (typically >5mm) on imaging; and failure of maximal medical therapy including anticoagulation, osmotic agents, and intubation with controlled ventilation (Saposnik et al., 2024; Ulivi et al., 2020). Timing is critical—surgery should be performed before irreversible brainstem injury occurs. Current guidelines recommend considering decompressive craniectomy in patients with large space-occupying lesions causing transtentorial herniation or progressive clinical deterioration despite maximal medical therapy (Ferro et al., 2017; Saposnik et al., 2024). Decisions should involve multidisciplinary discussion with neurosurgery and intensive care, considering patient age, premorbid functional status, extent of injury, and family preferences.

Special Populations and Situations

Pregnancy-related CVT requires careful management balancing maternal and fetal safety. LMWH is preferred anticoagulant throughout pregnancy and puerperium, as it does not cross placenta and has extensive safety data (Ferro et al., 2017; Saposnik et al., 2024). UFH is alternative but requires more frequent monitoring. VKAs are contraindicated in the first trimester due to teratogenicity and in late pregnancy due to fetal bleeding risk. DOACs should be avoided in pregnancy due to limited safety data and potential placental crossing. Anticoagulation should continue for at least 6 weeks postpartum, minimum 3 months total duration from CVT diagnosis (Saposnik et al., 2024). Breastfeeding is safe with LMWH or warfarin but should be avoided with DOACs.

COVID-19-associated CVT, particularly vaccine-induced immune thrombotic thrombocytopenia (VITT), requires specific management approaches. VITT is characterized by thrombocytopenia (typically platelet count <150,000/μL), thrombosis (often CVT), elevated D-dimer, and positive anti-platelet factor 4 (PF4) antibodies occurring 5-30 days after adenoviral vector COVID-19 vaccination (ChAdOx1 nCoV-19/AstraZeneca or Ad26.COV2.S/Johnson & Johnson) (Moraes Junior & Conforto, 2022). VITT management differs from typical CVT. Non-heparin anticoagulants should be used (direct thrombin inhibitors like argatroban or bivalirudin, or fondaparinux, or DOACs) to avoid potential heparin-induced thrombocytopenia-like syndrome (Moraes Junior & Conforto, 2022). Intravenous immunoglobulin (IVIG) 1g/kg/day for 2 days should be administered to reduce anti-PF4 antibody levels. (Moraes Junior & Conforto, 2022). Glucocorticoids may be considered in case of unavailability of IVIG (Moraes Junior & Conforto, 2022).

7. Prognosis and Outcomes

CVT prognosis has improved dramatically over recent decades with contemporary management. Mortality has declined from historical rates of 30-50% to current rates of approximately 5-10% in modern series (Ferro et al., 2019; Silvis et al., 2017). In the VENOST study of 1,144 patients, at the first month follow-up visit, 78.4% of patients had favorable outcome (mRS 0-1), 11.7% had minimal disability (mRS 2), and 10.0 % had poor outcome (mRS 3-5), with no deaths attributed to CVT at one month (Duman et al., 2017). Most deaths occur in the acute phase from brain herniation, status epilepticus, or systemic complications. Functional outcomes are generally favorable. Approximately 80% of CVT patients achieve functional independence (modified Rankin Scale 0-2) at long-term follow-up (Ferro et al., 2019; Silvis et al., 2017). However, approximately 10-20% experience unfavorable outcomes defined as death or significant disability (mRS 3-6). Most functional recovery occurs within the first few weeks, with minor further improvement up to 6 months (Ferro et al., 2019). Predictors of poor outcome have been consistently identified across multiple studies. Predictors of poor outcome include: coma or depressed mental status at presentation (GCS <9); involvement of deep venous system; large hemorrhagic infarctions with mass effect; central nervous system infection; and advanced age (Ferro et al., 2017; Gurram et al., 2024; Khan et al., 2020). Recurrent venous thromboembolism (VTE) represents an important long-term concern. The risk of a new cerebral or systemic venous thrombotic event after CVT is approximately 4 per 100 person-years, with most recurrences occurring within the first year (Silvis et al., 2017). The optimal duration of anticoagulation to prevent recurrence remains uncertain, with conflicting data on whether extended anticoagulation reduces recurrence risk (Silvis et al., 2017; Ferro et al., 2017). Patients with high thrombotic risk conditions may require permanent anticoagulation. Long-term sequelae affect a substantial minority of CVT survivors. Persistent headache is most common, occurring in approximately half of patients during follow-up, with severe headaches requiring bed rest or hospital admission persisting in approximately 14% (Silvis et al., 2017). More than half of survivors report subtle neuropsychological difficulties or depression (Silvis et al., 2017). Seizures occur in approximately 40-50% of CVT patients during the acute phase, though the rate of persistent seizure disorder requiring long-term AED treatment is not well quantified (Idiculla et al., 2020). About 6-10% of surviving patients have severe and permanent disability (Silvis et al., 2017). Although approximately 80% of patients recover without physical disability, many experience residual chronic symptoms impacting daily functioning (Silvis et al., 2017). Factors associated with reduced quality of life include persistent headache, cognitive complaints, seizures, and residual focal deficits. Approximately 20-40% of patients are unable to return to their prior working life due to these persistent symptoms.

Discussion

The comprehensive analysis of cerebral venous thrombosis (CVT) presented in this review synthesizes current evidence from international registries, clinical trials, and expert guidelines, revealing significant advances in understanding and managing this rare but potentially devastating cerebrovascular condition. The findings have substantial implications for clinical practice, particularly regarding diagnosis, anticoagulation strategies, and prognostic assessment. CVT accounts for less than 1% of all strokes, yet its true incidence may be underestimated due to underdiagnosis of mild cases or atypical presentations (Saposnik et al., 2024; Almegren, 2025). The identification of previously underrecognized risk factors such as anemia and obesity expands our understanding of CVT pathophysiology, suggesting that obesity-related chronic inflammation and endothelial dysfunction may contribute to hypercoagulability, while anemia may induce compensatory prothrombotic changes (Alimohammadi et al., 2022). The COVID-19 pandemic introduced new dimensions to CVT epidemiology and pathophysiology. Baldini et al. (2021) demonstrated through systematic review and meta-analysis that SARS-CoV-2 infection induces a prothrombotic state through multiple mechanisms including hypoxia, cytokine storm, endothelial dysfunction, and direct viral vascular injury, resulting in CVT incidence of approximately 0.08% among COVID-19 patients. Furthermore, vaccine-induced immune thrombotic thrombocytopenia (VITT) following COVID-19 vaccination represents a novel clinical challenge requiring specific diagnostic and therapeutic protocols distinct from conventional CVT management, particularly the avoidance of heparin due to its pathogenic role in VITT (Moraes Junior & Conforto, 2022). The heterogeneous clinical presentation of CVT constitutes the primary diagnostic challenge. Spadaro et al. (2021) emphasized the critical importance of rapid recognition in emergency department settings, where timely diagnosis significantly impacts outcomes. The possibility of CVT presenting as an isolated headache without focal neurological signs poses particular diagnostic difficulty, necessitating high clinical suspicion especially when thrombotic risk factors are present (Idiculla et al., 2020). Modern neuroimaging has substantially improved CVT detection, with magnetic resonance imaging and venography (MRV) remaining the diagnostic gold standard due to superior sensitivity and specificity (Dmytriw et al., 2018). Rosa et al. (2024) demonstrated that advanced techniques including susceptibility-weighted imaging and contrast-enhanced MRI increase detection sensitivity, particularly for cortical vein thrombosis that may be invisible on conventional sequences. This review highlights several critical clinical implications: maintaining high diagnostic suspicion for CVT in young patients with headache and thrombotic risk factors; utilizing advanced neuroimaging techniques for improved detection; considering DOACs as viable alternatives to warfarin for anticoagulation; individualizing treatment duration based on risk factor profiles; and implementing early risk stratification to optimize monitoring intensity and intervention timing. Future research should focus on definitively establishing optimal anticoagulation duration, refining endovascular intervention protocols, identifying biomarkers for early diagnosis and prognostic assessment, and developing strategies for preventing CVT in high-risk populations. The convergence of improved diagnostic capabilities, expanding therapeutic options, and enhanced understanding of pathophysiology positions the field to further improve outcomes for patients with this challenging condition

Conclusions

Cerebral venous thrombosis represents a distinctive form of stroke predominantly affecting young adults, particularly women of reproductive age, with complex and heterogeneous clinical presentations that frequently challenge diagnostic acumen. This comprehensive review demonstrates substantial progress in understanding CVT pathophysiology, diagnosis, and management over the past decade, translating into significantly improved patient outcomes with contemporary in-hospital mortality rates of 5-10% compared to historical rates exceeding 30%.

The advent of direct oral anticoagulants has revolutionized CVT treatment, with mounting evidence from randomized controlled trials and real-world studies establishing their safety and efficacy comparable to traditional vitamin K antagonists, while offering superior convenience and quality of life. Advanced neuroimaging techniques, particularly susceptibility-weighted imaging and contrast-enhanced MRI, have enhanced diagnostic sensitivity, enabling earlier detection and treatment initiation. Recognition of novel risk factors including anemia, obesity, COVID-19 infection, and vaccine-induced thrombotic thrombocytopenia has expanded our etiological understanding and prevention strategies.

Despite these advances, several critical knowledge gaps persist that warrant future investigation. The optimal duration of anticoagulation remains uncertain, with ongoing trials such as EXCOA-CVT expected to provide definitive guidance for balancing recurrence prevention against bleeding risk. The role of endovascular thrombectomy in severe CVT requires clarification through adequately powered randomized trials with standardized patient selection criteria and procedural protocols. The identification of reliable biomarkers for early diagnosis and accurate prognostic stratification would enable personalized treatment approaches and risk-adapted monitoring strategies. Furthermore, the long-term cognitive and functional outcomes of CVT survivors, particularly following severe presentations requiring decompressive craniectomy, necessitate systematic longitudinal investigation to optimize rehabilitation interventions and inform prognostic counseling.

Future research directions should prioritize development of validated clinical prediction models integrating demographic, clinical, radiological, and laboratory variables to facilitate early identification of high-risk patients requiring intensive monitoring and aggressive interventions. Exploration of novel therapeutic targets, including anti-inflammatory agents and neuroprotective strategies, may complement anticoagulation therapy to minimize secondary brain injury. Establishment of international registries with standardized data collection protocols would enable robust epidemiological surveillance, comparative effectiveness research, and identification of rare complications. Investigation of prevention strategies in high-risk populations, such as thromboprophylaxis protocols for pregnant women with hereditary thrombophilias or patients with active malignancies, could reduce CVT incidence.

The integration of artificial intelligence and machine learning algorithms into diagnostic workflows holds promise for enhancing early CVT recognition from clinical presentations and neuroimaging studies, potentially reducing diagnostic delays that adversely impact outcomes. Development of patient-centered outcome measures beyond traditional mortality and modified Rankin Scale assessments, incorporating health-related quality of life, cognitive function, and return to work or education, would provide a more comprehensive evaluation of treatment effectiveness.

In conclusion, cerebral venous thrombosis management has evolved from a poorly understood condition with dismal prognosis to a treatable cerebrovascular disorder with favorable outcomes when promptly recognized and appropriately managed. Continued research addressing remaining knowledge gaps, coupled with implementation of evidence-based guidelines and multidisciplinary collaborative care models, will further optimize outcomes for patients affected by this challenging condition. The convergence of advanced diagnostic technologies, expanded therapeutic armamentarium, and deepening pathophysiological insights positions the field to achieve continued progress in reducing CVT-related morbidity and mortality while improving long-term functional and cognitive outcomes for survivors.

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