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Review Article

Cerebral Venous Thrombosis: Anticoagulation Strategies and Recanalisation Rates

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Abstract

Background: Cerebral venous thrombosis (CVT) is an uncommon but treatable stroke subtype causing headache, seizures, focal deficits or coma. Anticoagulation is its cornerstone, yet optimal agent, duration and role of recanalisation remain debated.

Objective: To review anticoagulation strategies for CVT, including heparin, vitamin K antagonists, direct oral anticoagulants, endovascular therapy, and recanalisation, plus special populations.

Methods: Narrative review of randomised trials, cohorts, registries and guidelines.

Findings: Heparin remains first-line even with haemorrhagic infarction. RE-SPECT CVT showed dabigatran comparable to warfarin, and ACTION-CVT supported direct oral anticoagulants in practice. TO-ACT found no added benefit from endovascular therapy in severe disease. Recanalisation is frequent but correlates poorly with functional outcome.

Conclusions: Heparin followed by three to twelve months of oral anticoagulation, guided by provoking factors, remains standard care, with endovascular therapy reserved for deterioration and tailored approaches needed in pregnancy and thrombocytopenic thrombosis.

Keywords: Cerebral venous thrombosis; Anticoagulation; Direct oral anticoagulants; Recanalisation; Endovascular thrombectomy

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Introduction

Cerebral venous thrombosis (CVT) is an uncommon cerebrovascular disorder in which thrombus forms within the cerebral veins or dural venous sinuses, impairing venous drainage and, when collateral pathways fail, raising venous pressure enough to cause parenchymal oedema, haemorrhagic infarction or intracranial hypertension [1]. It accounts for a small fraction of all strokes but disproportionately affects younger adults and women, particularly around pregnancy, the puerperium and use of combined oral contraceptives [2].

Population-based ascertainment suggests CVT is more common than earlier hospital-based series implied, with incidence estimates now approaching 1.3 per 100,000 person-years and rising further where MRI and CT venography are readily available [3,4].

The International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT), a prospective cohort of 624 patients, remains the foundational description of presentation, treatment and prognosis, reporting death or dependency in roughly 13% of patients and complete recovery in about 79% [5]. Common presenting features across that and subsequent cohorts include headache, seizures, focal motor or sensory deficits, papilloedema from raised intracranial pressure, and, less commonly, encephalopathy or coma reflecting extensive deep venous involvement. Recognised provoking factors span hormonal exposures (pregnancy, puerperium, combined oral contraception), inherited or acquired thrombophilia, malignancy, infection, dehydration, and mechanical or iatrogenic causes such as head injury or central venous catheterisation, although a meaningful minority remain unprovoked despite thorough evaluation [2].

Anticoagulation has been the cornerstone of treatment since the first small randomised trials in the early 1990s, but the evidence base has since expanded considerably: trials of direct oral anticoagulants, an endovascular therapy trial, large observational registries, and a growing literature on recanalisation and its prognostic meaning. This review synthesises that evidence, organised around acute anticoagulation, oral anticoagulant choice, endovascular therapy, recanalisation, treatment duration, outcome prediction, and special populations including pregnancy and vaccine- or infection-associated thrombosis.

Acute-Phase Anticoagulation

Unfractionated heparin and low-molecular-weight

heparin (LMWH) are the standard acute treatments for CVT, including in patients with pre-existing haemorrhagic venous infarction, because the risk of thrombus propagation and clinical deterioration without anticoagulation is judged to exceed the risk of haemorrhage expansion. This approach rests on two small but influential randomised trials. Einhupl and colleagues randomised 20 patients to intravenous heparin or placebo and stopped the trial early after an interim analysis favoured heparin, with three deaths in the placebo group and none in the treatment group [6]. De Bruijn and Stam subsequently randomised 60 patients to subcutaneous LMWH (nadroparin) or placebo; although not statistically significant, the trend again favoured anticoagulation, and a pooled analysis of both trials supported a clinically meaningful reduction in death or dependency [7]. These trials, though underpowered individually, established heparin as standard care and are the basis for guideline recommendations from the European Federation of Neurological Societies, the European Stroke Organization, and the American Heart Association [8,9,10]. LMWH is generally preferred over unfractionated heparin for its more predictable pharmacokinetics and lower monitoring burden, reserving unfractionated heparin for patients at high bleeding risk or facing possible early intervention.

Oral Anticoagulation: Vitamin K Antagonists and Direct Oral Anticoagulants

Following acute-phase heparin, vitamin K antagonists (VKAs) such as warfarin have long been the default oral therapy, targeting an INR of 2.0-3.0. The RE-SPECT CVT trial was the first randomised comparison of a direct oral anticoagulant (DOAC) against dose-adjusted warfarin in CVT, enrolling 120 patients after a lead-in period of parenteral anticoagulation. Dabigatran etexilate showed a similar rate of recurrent venous thrombosis and a numerically lower rate of major bleeding compared with warfarin, without loss of efficacy on recanalisation [11,12].

These findings have been reinforced by the ACTION-CVT registry, an international multicentre study of over 800 patients comparing DOACs (chiefly rivaroxaban and apixaban) with warfarin in routine practice; DOAC-treated patients had similar rates of recurrent thrombosis and death, with fewer major haemorrhages [13]. Smaller single-centre experiences and systematic reviews of apixaban have reported comparable outcomes, supporting DOACs as a reasonable alternative once patients are stabilised on parenteral anticoagulation [14]. Current guidance still favours VKAs or heparin in patients with antiphospholipid syndrome or other conditions in which DOAC efficacy is less certain, but for most patients a DOAC is now an accepted, guideline-endorsed option [10,9].

Table 1: Key randomised and registry evidence informing anticoagulation strategy in cerebral venous thrombosis [6,7,11,13,15].				
Study	Design	N	Comparison	Key result
Einhupl 1991	RCT (stopped early)	20	IV heparin vs placebo	Fewer deaths with heparin
de Bruijn/Stam 1999	RCT	60	LMWH vs placebo	Trend favouring LMWH
RE-SPECT CVT 2019	RCT	120	Dabigatran vs warfarin	Comparable efficacy, less bleeding
ACTION-CVT 2022	Multicentre registry	845	DOAC vs warfarin	Similar recurrence, fewer haemorrhages
TO-ACT 2020	RCT (stopped for futility)	67	Endovascular + standard vs standard care	No added benefit, more haemorrhage

Endovascular Therapy for Severe Cerebral Venous Thrombosis

Endovascular mechanical thrombectomy and local thrombolysis have been proposed for patients who deteriorate despite anticoagulation or who present with severe disease, including coma or extensive deep venous system involvement. The TO-ACT trial randomised 67 patients with severe CVT (assessed by clinical or

radiological criteria) to endovascular treatment plus standard care versus standard care alone; the trial was stopped early for futility, with no difference in the proportion achieving a good functional outcome and a signal toward more intracranial haemorrhage in the endovascular group [15]. Meta-analyses of predominantly observational thrombectomy series report high technical recanalisation rates and improvement in many treated patients, but these series are subject to substantial selection and publication bias and lack a comparator arm [16]. Taken together, the evidence base does not support routine endovascular therapy in CVT; current guidelines reserve it for patients who deteriorate neurologically despite adequate anticoagulation, ideally within a multidisciplinary and, where feasible, trial context [10,9].

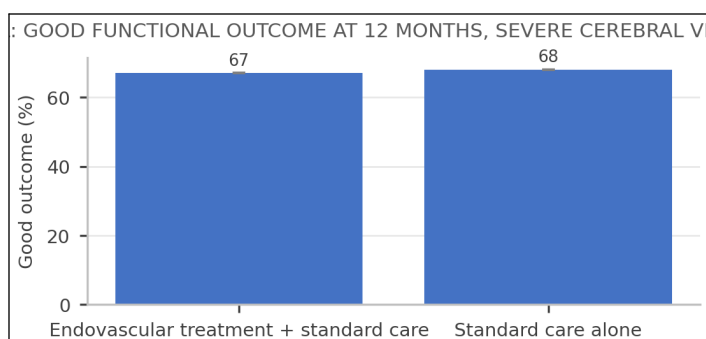


Figure 1: Proportion of patients with severe cerebral venous thrombosis achieving a good functional outcome with endovascular treatment plus standard care versus standard care alone in the TO-ACT trial [15].

Recanalisation Rates and Their Relationship to Outcome

Recanalisation of the thrombosed vein or sinus is common after anticoagulation, with most improvement occurring within the first three to four months and comparatively little further change thereafter. In a cohort using systematic follow-up imaging, complete or partial recanalisation was seen in the substantial majority of patients by six months, but the timing and degree of recanalisation correlated only weakly with functional outcome at follow-up [17]. The RE-SPECT CVT imaging

substudy similarly found recanalisation rates of roughly four in five sinuses or veins across both the dabigatran and warfarin arms, again with a limited relationship between recanalisation status and clinical recovery [12]. The practical implication is that persistent occlusion on follow-up imaging should not, by itself, be used to extend or intensify anticoagulation, and conversely, complete recanalisation does not by itself justify early cessation of treatment; clinical and risk-factor assessment should drive duration decisions rather than imaging appearance alone [10].

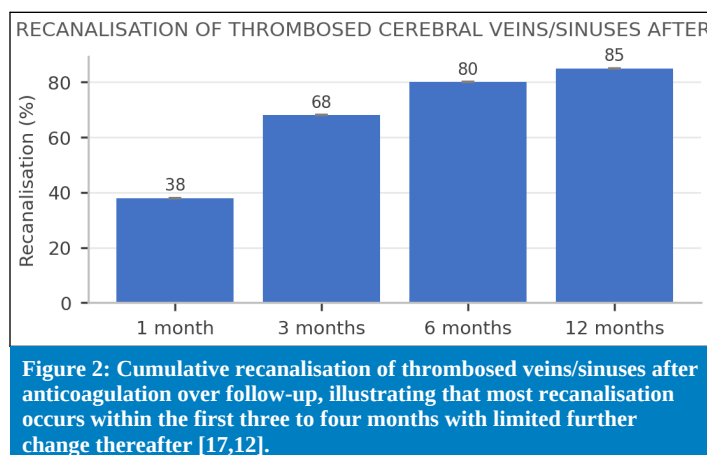


Figure 2: Cumulative recanalisation of thrombosed veins/sinuses after anticoagulation over follow-up, illustrating that most recanalisation occurs within the first three to four months with limited further change thereafter [17,12].

Duration of Anticoagulation

Guideline recommendations on treatment duration are derived largely from clinical experience and observational cohorts rather than dedicated randomised comparisons of duration. Typical guidance is three to six months of oral anticoagulation for CVT provoked by a transient risk factor (such as pregnancy, the puerperium, or oestrogen-containing contraception), six to twelve months for unprovoked CVT, and longer or indefinite anticoagulation for patients with recurrent venous thromboembolism, severe inherited thrombophilia, or active malignancy [8,9,10]. The EXCOA-CVT cluster-randomised trial protocol was designed specifically to test whether extending oral anticoagulation beyond the conventional period reduces recurrence

without excess bleeding, reflecting the continued uncertainty in this area [18]. Recurrence of CVT itself is uncommon, but patients with CVT also carry an elevated long-term risk of other venous thromboembolic events, which some guidance suggests should factor into duration decisions alongside the thrombophilia work-up. Until definitive duration trials report, decisions are individualised, weighing provoking factors, thrombophilia results, recanalisation status (with the caveats above), and bleeding risk.

Outcome Predictors and Risk Stratification

Because most patients with CVT recover well, risk stratification is useful for identifying the minority who need closer monitoring or more aggressive intervention. Using the ISCVT cohort, Ferro and colleagues derived and validated a risk score assigning points for malignancy, coma, mental status disturbance, male sex, intracranial haemorrhage, and thrombosis of the deep venous system, which reliably separated patients into low-, intermediate- and high-risk groups for death or dependency [19]. This score, alongside clinical features captured in the original ISCVT description such as altered consciousness at presentation and rapid neurological deterioration, remains widely used to inform intensity of monitoring, need for intensive care, and threshold for considering endovascular rescue therapy [5,10].

Special Populations: Pregnancy and Puerperium

Pregnancy and the six-week puerperium carry an increased risk of CVT, reflecting the procoagulant state of late pregnancy and delivery. A pooled systematic review found that most pregnancy-associated CVT occurs post-partum, that presentation and outcome are broadly similar to non-pregnancy-associated CVT, and that with anticoagulation most women make a good recovery and can safely have further pregnancies with prophylactic LMWH [20]. A more recent systematic review and meta-analysis of pregnancy- and postpartum-associated

CVT confirmed a favourable prognosis relative to other stroke subtypes when anticoagulation is instituted promptly, while emphasising that LMWH, rather than VKAs or DOACs, remains the anticoagulant of choice throughout pregnancy [21]. Guidelines concur that pregnancy itself is not a contraindication to standard-dose heparin-based treatment and that mode of delivery should be guided by obstetric rather than neurological factors in most cases [10].

Table 2: Variables in the ISCVT risk score for predicting death or dependency after cerebral venous thrombosis [19].

Predictor	Direction of association	Points
Malignancy	Increases risk	2
Coma	Increases risk	2
Mental status disturbance	Increases risk	1
Male sex	Increases risk	1
Intracranial haemorrhage	Increases risk	1
Deep venous system thrombosis	Increases risk	2

Special Populations: COVID-19 and Vaccine-Induced Thrombotic Thrombocytopenia

Two distinct phenomena emerged during the COVID-19 pandemic. First, SARS-CoV-2 infection itself was associated with CVT, generally at low absolute frequency but with a case-fatality rate higher than in non-COVID CVT in some series, attributed to a systemic prothrombotic and inflammatory state [22,23]. Second, adenovirus-vector COVID-19 vaccines were associated with a rare but distinctive syndrome of vaccine-induced immune thrombotic thrombocytopenia (VITT), characterised by thrombosis (frequently cerebral venous) with concurrent thrombocytopenia and antibodies against platelet factor 4, mechanistically resembling autoimmune heparin-induced thrombocytopenia [24,25]. Because heparin can potentiate the underlying antibody-platelet interaction in VITT, American Heart Association/American Stroke Association guidance recommends avoiding heparin where VITT is suspected or

confirmed, favouring non-heparin anticoagulants such as argatroban, danaparoid, fondaparinux or a DOAC, together with intravenous immunoglobulin and avoidance of platelet transfusion unless needed for life-threatening bleeding [26]. These episodes also transiently altered population-level CVT ascertainment, an effect visible in national inpatient trend data spanning the pre-pandemic and pandemic periods [27,4].

Conclusion

The evidence base for CVT management has matured substantially since the first small heparin trials of the early 1990s. Heparin, followed by oral anticoagulation, remains the backbone of treatment, and the RE-SPECT CVT trial and the ACTION-CVT registry together support direct oral anticoagulants as a reasonable, guideline-endorsed alternative to vitamin K antagonists for most patients. The TO-ACT trial showed no benefit from routine endovascular therapy in severe disease, reserving that option for clinical deterioration despite adequate anticoagulation. Recanalisation, while frequent, is a poor surrogate for functional outcome and should not by itself dictate treatment duration, which instead should follow individualised assessment of provoking factors, thrombophilia and bleeding risk, informed by validated risk scores such as the ISCVT score. Pregnancy-associated and thrombocytopenic (VITT-related) CVT each require anticoagulant choices tailored to their distinct pathophysiology. Dedicated trials of anticoagulation duration and of DOAC use in higher-risk subgroups remain the most pressing unmet needs.

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