

Cerebral venous thrombosis

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Summary

Cerebral venous thrombosis (CVT) has an incidence of 1.32/100,000/years in high-income countries, and higher in middle- and low-income countries. CVT is more frequent in infants and children young adults and females, especially during pregnancy/puerperium. CVT are now being diagnosed with increasing frequency because of the increased awareness and higher use of magnetic resonance imaging (MR) for investigating patients with acute and subacute headaches and new onset seizures. CVT rarely present as a stroke syndrome. Their most frequent presentations are isolated headache, intracranial hypertension syndrome, seizures, a lobar syndrome and encephalopathy. The confirmation of the diagnosis of CVT relies on the demonstration of thrombi in the cerebral veins and/or sinuses by MR/MR venography or veno CT. The more frequent risk factors/associated conditions for CVT are genetic prothrombotic conditions, antiphospholipid syndrome and other acquired prothrombotic diseases, including cancer, oral contraceptives, puerperium and pregnancy, infections and trauma. The prognosis of CVT is in general favorable, as acute death rate is below 5% and only 15% of the patients remain dependent or die. Treatment in the acute phase includes management of the associated condition, anticoagulation with either low molecular weight or unfractionated heparin, treatment of intracranial hypertension, prevention of recurrent seizures and headache relief. In patients in severe condition on admission or who deteriorate despite anticoagulation, local thrombolysis or thrombectomy is an option. Decompressive surgery is lifesaving in patients with large venous infarcts or hemorrhage with impending herniation. After the acute phase, patients should be anticoagulated for a variable period of time, depending on their inherent thrombotic risk. CVT patients may experience recurrent seizures. Prophylaxis with anti-epileptic drugs is recommended after the first seizure, in those with hemispheric lesions. There are several ongoing multicenter registries and trials, which will improve evidence-based and patient-centered management of CVT in the near future.

Definition

While for neurologists, thrombosis of the dural venous sinus or of the cerebral veins are regarded as a special type of stroke, for vascular surgeons and hematologists, they are considered as a

venous thrombosis in a special anatomical location [1]. Cerebral vein and dural sinus thrombosis (CVT) are in fact an example of venous thrombosis in an uncommon location, in this regard similar to splanchnic venous thrombosis. CVT are also a venous thrombosis with a special pathophysiology, due to the lack of a role for hydrostatic gravitational pressure in CVT, in contrast to what happens in the much more common deep venous thrombosis of the lower limbs.

Contrasting CVT with arterial stroke, a few key aspects are apparent:

- CVT are less common but they can be easily missed and their diagnosis is often delayed;
- CVT affects much younger patients with a female predominance (figure 1);
- CVT has in general a non-apoplectic onset, rarely present as a stroke syndrome, but has a wider spectrum of clinical presentation syndromes;
- CVT has multiple risk factors and associated conditions, which are different from those of arterial stroke;
- CVT has a different treatment, similar to systemic deep venous thrombosis, consisting mainly of parenteral heparin followed by oral anticoagulation;
- CVT has a much more favorable outcome

Epidemiology

CVT is less frequent than ischemic stroke and also than intracerebral or subarachnoid hemorrhage. The older studies of CVT prevalence were autopsies studies. They reported a high prevalence of 1–9% CVT as a post-mortem finding often asymptomatic during life [2]. A mortality study performed in the UK from 1952 to 1961 reported an average of 22 cases of fatal CVT annually and a death rate due to CVT of 0.39 per million [3]. These high figures reflect selection bias for severe fatal cases and high rates of CVT associated with infections.

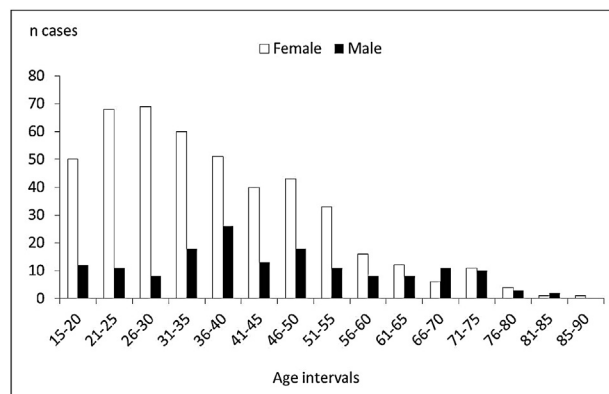


FIGURE 1

Age and gender distribution in the International Study on Dural Sinus and Cerebral Vein Thrombosis cohort. Females outnumber males in fertile age

More recent studies were mainly hospital bases series. In a cooperative study of Neurology centers in Portugal, a CVT incidence of 0.22/100,000/year was reported [4]. A higher incidence was reported in Isfahan, Iran (1.23/100,000/year) [5]. The epidemiological study of CVT with the more valid methodology was performed in the Netherlands and found an overall incidence of 1.32/100,000/year and of 2.78 for women between the ages of 31 and 50 [6]. The higher incidence found in this study probably reflects a higher detection rate and a more complete case ascertainment. This incidence is similar to that of bacterial meningitis in adults. Higher incidences of CVT are found in infants and children, in young adults and in females. In contrast to other stroke subtypes, the incidence of CVT decreases with age. A systematic review including of 8829 CVT patients from 74 series with more than 40 subjects found an average age of 32.9 years and 64.7% of women [7]. CVT is also more frequent in low-middle income countries, in particular in those with high pregnancy rates. In fact, CVT represented 3% of 2000 strokes in a Stroke Registries in Mexico [8]. Rates of CVT during pregnancy also show high: 11.6/100,000 deliveries in the USA [9] and more than half of all strokes among pregnant women (136/240 [57%]) in Mexico [10]. A higher incidence (0.64/100,000) was also reported in infants and children < 18 years in Canada [11]. Due to increased awareness and easier access to magnetic resonance imaging (MR) for investigating patients with acute and subacute headaches and new onset seizures, CVT are now being diagnosed with increasing frequency. A systematic review of CVT series with more than 40 patients showed a clear trend in declining mortality in patients with CVT over time [12]. The frequency of focal neurological deficits and coma also decreased significantly over time. Declining in mortality can be due to better management, a decrease in septic CVT, but most probably is mainly due to the identification of less severe cases by MRI. There are however several reasons to suspect that the incidence of CVT is still underestimate. CVT have a more varied clinical presentation than other stroke types and hence they are more difficult to recognize. In particular, in the two extremes of their clinical spectrum of severity, CVT may easily be missed. CVT patients complaining only of headache may usually have a benign auto-limited course [13] and CVT will not be diagnosed unless CT plus CT venography or MR plus MR venography are performed. On the other hand, in severely ill or terminal patients (e.g. cancer), headache may be absent [14] and new or worsening neurological signs may be attributed to other causes (metastatic, metabolic or infectious) and neuroimaging to rule out CVT may deemed not necessary.

Anatomy of the brain venous system

The cerebral venous drainage pattern does not correspond to cerebral arterial territories and is often asymmetric (figure 2). The variability of the superficial Sylvian vein and anastomotic

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