Cerebral Venous Thrombosis
Epidemiology in Change

Turgut Tatlisumak, MD, PhD; Katarina Jood, MD, PhD; Jukka Putaala, MD, PhD, MSc(Stroke)

See related article, p 2180.

Cerebral venous thrombosis (CVT) refers to local clot formation and occlusion of intracranial venous structures, including the dural venous sinuses, cortical veins, and the proximal part of the jugular veins, leading to an acute or delayed manifestation with a large variety of symptoms and signs, making the diagnosis difficult. Diagnostics have improved after introduction of noninvasive imaging modalities, resulting in increased number of patients detected as well as improved outcomes partly because of recognition of less severe cases. CVT is still an underinvestigated disease, and therefore, new studies from different parts of the world are most welcome for increasing our currently modest knowledge.

In this issue of the journal, Devasagayam et al report on their findings from a well-defined geographical region of Australia (Adelaide, South Australia) inhabited by almost 1 million adults. Briefly, they retrospectively attempted to identify all adult CVT cases treated at all 7 public hospitals in their region between years 2005 and 2011 and made 3 distinct observations: (1) they could confirm 105 adult cases, leading to an incidence of 15.7 cases per million inhabitants annually, which is the highest figure ever reported; (2) they searched for CVT cases through electronic hospital discharge diagnosis records by using diagnostic codes for CVT, but also used a phrase (for text variations containing venous thromb) in searching through their radiology repository, which delivered 40 (38%) additional cases that could not be identified via the discharge diagnosis search; and (3) they found almost equal sex distribution (52% females) that contradicts the results of all previous studies. Their study, despite having the typical limitations of retrospective registries, offers some new insights.

The incidence of CVT is not well-studied. Earlier studies reported low incidences, more severe presentation, and worse outcomes, including higher mortality rates most likely because mild cases went undetected. After introduction of noninvasive imaging modalities for CVT diagnostics and improvement of awareness among physicians, the reported incidences increased steadily over time. For instance, a retrospective hospital-based study from Saudi Arabia covering a period of 1985 to 1994 estimated an incidence of <10 cases per million per year, a prospective hospital-based study that detected 122 patients between 2001 and 2004 from Isfahan, Iran, reported 12.3 per million, a retrospective multicenter study from the Netherlands covering 94 patients during 2008 to 2010 ended up reporting 13.2 per million person-years, and a more recent prospective single-center work from Hamadan, Iran, included 151 cases diagnosed between 2009 and 2015 and found an incidence of 13.5 cases per million per year.

The article by Devasagayam et al in this issue continues this trend with an even higher incidence of 15.7 per million inhabitants per year and, yet, may be underestimated the real incidence because at least some private hospitals could not be covered. Their findings do not alone prove that Australia has a higher incidence for CVT, but suggest that the better we investigate, the higher incidence rates we find for CVT. Finding CVT patients through imaging repositories by using key words is an interesting approach, used also previously by Iranian investigators (although not described in detail by them). It seems this approach was rather fruitful. CVT indeed may be recorded with several diagnoses and may be difficult to retrieve from hospital records. One concern here is that the Adelaide region healthcare systems are offering stroke care in 7 public hospitals and additionally in some private hospitals for a relatively small population residing in a geographically limited area. As there are 15 new cases annually, this means each hospital and stroke team will see only few patients, which is clearly too few for building up and maintaining quality. This may well be a reason why so many patients were miscoded in discharge diagnosis registry. It may be extremely valuable to concentrate the diagnostics and care of young stroke patients (including CVTs) to few centers where high competence can flourish over time.

Although reported incidence rates are on rise, mortality rates are declining. This change may reflect both better diagnostics for mild cases and improved management strategies. Pulmonary embolisms described as a dreadful complication in old reports have disappeared in the era of anticoagulants. Currently, early deaths are commonly caused by increased intracranial pressure, whereas late mortality is often caused by malignity underlying the CVT. Although CVT mortality was as high as 50% half a century earlier, more recent reports indicate a mortality rate of 5% to 10%.

Despite the fact that most CVT patients survive their disease, long-term prognosis of CVT is poorly investigated. Few reports indicate that ≈80% to 90% of the patients achieve a modified Rankin Scale score of 0 to 1, and few patients remain with severe disabilities when measured with modified Rankin Scale scores.
Scale scores. Recurrent venous events, including CVTs, seem to occur in ≈2% of the survivors annually.⁷⁻¹⁰ However, chronic headaches, failure to thrive, and fatigue are common consequences found in over half of the survivors.¹⁰ One fourth of the survivors could not return to professional life on the basis of CVT.¹⁰

A recent systematic analysis showed that the proportion of females among CVT patients has increased over the last decades, now being ≈70%.¹¹ The excess of female patients can be mainly explained with hormonal factors because even one third of the child-bearing-aged females in western countries use oral contraceptives, and their portion is about half among all CVT patients.¹¹ The contraceptive preparations used in Australia are hardly different regarding their consistency compared with other industrialized countries. The likely explanation for surprisingly high proportion of male patients in the study of Devasagayam et al is,¹ therefore, a chance finding.

In summary, CVT epidemiology is not well-investigated, and our knowledge comes from rather small mostly single-center studies. In the future, we need to unite forces and design multinational large preferably prospective studies to increase our knowledge on many facets of global CVT epidemiology. We do not know whether there exist genuine differences in incidence, disease severity, or other important aspects of the disease between geographical, ethnic, or socioeconomic patient groups, whether these differences stem from genetic or environmental factors (such as high existence of untreated facial and otic bacterial infections in low-income regions, hot climate leading to dehydration, seasonal variations again because of infective or temperature-dependent effects, differences in hormonal factors, or even factors we are not well aware yet), and what portion of the CVT cases are easily preventable with population-based approaches. There are ongoing efforts for creating multicenter/multinational databases of CVT patients, as well as one large global study for exploring CVT genetics. All CVT researchers are encouraged to participate in these efforts because it seems to be the only way to decipher the many important but yet unknown aspects of this fascinating disease.

Disclosures

None.

References


Key Words: Editorials • cerebral venous thrombosis • dural sinus thrombosis • epidemiology • incidence • long-term outcomes • mortality