Cerebral Venous Thrombosis
Another Heparin Controversy

Magdy Selim, MD, PhD

See related article, p 298.

Results from clinical studies and advances in radiological diagnosis during the past 20 years have significantly altered the management of patients with cerebral venous thrombosis (CVT), with resultant improvement in overall prognosis and decreased mortality. Although the efficacy of anticoagulation in CVT has not been unequivocally proven, it is widely used as the mainstay therapy. There is a pathophysiological rationale to recommend the use of anticoagulation in CVT. Occlusion of cerebral venous system impairs blood outflow from the brain, resulting in increased intracranial and capillary pressure and subsequently intracerebral hemorrhage (ICH). The use of anticoagulation can theoretically prevent thrombus propagation, facilitate recanalization of the occluded venous sinus, and improve venous outflow.

Scattered case reports and series in the literature described the successful use of heparin in CVT since the 1940s. In the early 1990s, Einhäupl et al performed the first randomized controlled study: 20 patients with CVT were randomized to a placebo versus heparin. Patients treated with heparin showed significant improvement; all of the heparin-treated patients survived, and 80% had a complete clinical recovery after 3 months. No new cases of ICH occurred after initiation of heparin. Einhäupl et al also reported their retrospective experience in 43 patients with CVT with ICH; 27 patients were treated with intravenous heparin after the ICH. Of these, 15% of patients died compared with 69% of patients who did not receive heparin, and 52% of patients completely recovered. The authors concluded that anticoagulation is an effective treatment in patients with CVT, and that ICH is not a contraindication to anticoagulation. De Bruijn and Stam followed up by a larger randomized double-blinded placebo-controlled multicenter trial; 30 patients were randomized to subcutaneous nadroparin (180 U/kg per 24 hours), and 29 patients were treated with intravenous heparin after the ICH. Of these, 15% of patients died compared with 69% of patients who did not receive heparin, and 52% of patients completely recovered. The authors concluded that anticoagulation is an effective treatment in patients with CVT, and that ICH is not a contraindication to anticoagulation.

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considerable. He argues that anticoagulation for CVT is not
evidence based to be effective or safe.

The study by Cundiff has several limitations that signifi-
cantly limit the interpretation of his findings and conclusions.
Despite the author’s reliance on personal communications
to obtain unpublished data on outcome and anticoagulation
status from previously published studies, only a handful of
studies provided part or all of the data. Similarly, few stud-
ies reported data on the recurrence of venous thrombosis. In
addition, calculating the rate of recurrence per month is less
than ideal given that the follow-up duration in various studies
varied from <3 months to >3 years. In addition, the impact of
selection bias on the choice of therapy in various patients can-
not be either ascertained or ignored. Finally, there are several
missing important data elements from Cundiff’s study, such as
the cause and risk factors for death in anticoagulated patients
(Table 2); one needs to know to ascertain that their death was
related to anticoagulation.

Despite these limitations, Cundiff indeed raises valid con-
cerns and questions of clinical and therapeutic importance
that are yet to be fully answered. The use of anticoagulants in
patients with CVT poses a real risk: ICH. There is paucity of
data about the de novo occurrence or worsening of ICH after
anticoagulant treatment in a larger number of patients to obtain
more robust estimation of the risk. Similarly, reliable data
about the subgroups of patients with CVT who may or may
not benefit from anticoagulation therapy are lacking. Should
the extent, number, and location of the affected sinuses and
the identified cause(s) for CVT influence the decision-making?
Perhaps the most intriguing aspects of Cundiff’s review are
his findings that in-hospital death rate was lower in antico-
agulated patients (9% versus 14%; Table 1), and that patients
receiving posthospitalization anticoagulants had lower death
rates (1.6% versus 6.9%; Table 4); that is, anticoagulation
decreases mortality.

Therefore, the question becomes whether anticoagulants
should be avoided in the name of safety in the absence of
large-scale randomized trials and statistical significance. Are
you willing to embark on a new trial that includes a placebo
group? Is there a role for newer anticoagulants in CVT? What
about antiplatelet therapy? Needless to say, the existing evi-
dence-based guidelines for management of CVT would ben-
efit from more evidence.

Disclosures
None.

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