Evidence Basis for Anticoagulants for Cerebral Sinus Venous Thrombosis? Reply by David K. Cundiff

Not only did the International Study on Cerebral Venous Thrombosis (ISCVT) articles fail to provide evidence against the hypothesis that anticoagulants reduce morbidity and mortality in patients with CVT, but they provided solid evidence against using anticoagulants for CVT.

I agree with the ISCVT authors that in observational studies, risk factors present in treated and untreated patients may confound any outcome comparison. Unfortunately, the ISCVT articles published so far have not compared anticoagulated versus unanticoagulated cohorts with respect to the prevalence of risk factors (eg, baseline intracerebral hemorrhage [ICH], presentation with stupor or coma, age, etc) in relationship to clinical outcomes (eg, death and disability). Surely will include the imminent publication of these data mentioned by Dr Ferro and Canhão.

The ISCVT authors said that insufficient variation existed for an appropriate comparison of patients who were anticoagulated (n=520 treated with full-dose heparin) versus unanticoagulated (n=104, including no antithrombotic drug=23, antiplatelet agents=50, low dose heparin=23, vitamin K antagonists=28, and thrombolysis=3) due to lack of statistical power. I disagree. They used exactly this comparison to try to show a possible benefit of full-dose heparin on death and dependency at the end of outpatient follow-up (an inappropriate clinical outcome in relation to full-dose heparin in hospital): “We found a nonsignificant difference in outcome in favor of the patients who were anticoagulated in therapeutic doses in the acute phase (66/520 [12.7%] dead/dependent versus 19/104 [18.3%]; HR 0.73; 95% CI, 0.44 to 1.21).”1 Consequently, the ISCVT authors have no basis to object to my appropriate hospital mortality comparison of fully heparinized patients relative to those not fully heparinized (full-dose heparin, 25/520 [4.8%] dead versus no full-dose heparin, 2/104 [1.92%]; odds ratio [OR] 2.5; 95% confidence interval, 0.58–10.7; P=0.20).2,3

The ISCVT authors challenged my inference that the only patient who died who received no antithrombotic drug was the only patient first diagnosed with CVT at autopsy. I stand corrected. They clarified that a 37-year-old woman had ICH at presentation and received full-dose heparin. CVT was confirmed in this patient only at autopsy. Despite an autopsy, it was not known if the ICH had increased from baseline.2 Indeed, of the 25 patients who received full-dose heparin and died, 16 patients had documented new brain lesions after receiving heparin. However, out of 104 patients who did not receive full-dose heparin, 1 patient who received no antithrombotic drug died. She died of sepsis (ICH but no herniation). The only nonheparinized patient who died of brain herniation and ICHs had received an antiplatelet drug.

Finally, about the implications for anticoagulation treatment of Hillary Clinton, I agree with the ISCVT authors that headache alone, as clinical presentation, forecasts a very good prognosis at any age. My point is that the ISCVT data indicate an alarming risk of fatal bleeding with anticoagulants, especially in patients ≥65 years. Of 41 patients who were ≥65 years who received full-dose heparin, 4 died in hospital, 3 of whom presented with ICH. Of 37 patients who were ≥65 years and were given vitamin K antagonists during follow-up, 2 died of bleeding complications.

Currently, the American Heart Association/American Stroke Association guidelines recommending anticoagulants for CVT make it risky for physicians treating CVT patients to avoid heparin and oral anticoagulants. If an unanticoagulated patient deteriorates or dies, as some will, the doctor may face a malpractice suit. However, the ISCVT data should guide physicians to avoid full-dose anticoagulants or other antithrombotic drugs for CVT.

Disclosures

None.

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Stroke. 2013;44:e151; originally published online October 1, 2013; doi: 10.1161/STROKEAHA.113.003244

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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