Banning Anticoagulation in Stroke or Consequence of Poor Study Design

To the Editor:

We read with great interest the review from H.P. Adams1 who critically re-evaluates individual aspects of well-known and often-discussed studies on anticoagulation in acute stroke. These studies do not exhibit a net benefit of anticoagulant use with regard to the criteria safety, mortality, morbidity, prevention of stroke recurrence and late outcome. The author emphasized the differences among the individual studies with regard to sample sizes, time-to-start of therapy (extending up to 48 hours after stroke onset), protocols for dosages and controls of anticoagulants used and the route of administration leading to a distinct criticism of major meta-analysis published. In addition, prominent shortcomings such as the missing baseline brain imaging studies in the dominating IST and CAST trials and the lack of any efforts to differentiate among stroke subtypes with gross under representation of embolic mechanisms are mentioned. However, despite these shortcomings, H.P. Adams concludes that he sees no indication for anticoagulation in acute stroke and suggests the future role of anticoagulants will be very limited.

In our view this conclusion is premature and not accepted by many “stroke experts” in institutions where advanced diagnostic techniques and neuro-monitoring are available. So far the albeit limited data available from these trials reveals statistically significant advantages of anticoagulation in the prevention of deep venous thrombosis, pulmonary embolism, as well as of early recurrent stroke. It is likely that a supposed increase in risk of bleeding complications is biased by restrictions of IST and CAST which do not reflect standards of acute stroke management in major European and North American hospitals. These standards include high-quality brain and vascular imaging (CCT, MRI, ECD, TCD), cardiac diagnostics (ECG-monitoring, TTE and TEE) and monitoring of blood pressure, metabolic and relevant coagulation blood parameters performed within days after stroke onset by trained neuroradiologists, cardiologists, angiologists, and stroke unit teams. Such techniques have been shown to be able to reduce symptomatic hemorrhagic transformation and bleeding complications in patients treated with rtPA in acute stroke trials even if the time window was extended beyond 3 hours.2 They may similarly improve the benefit/risk ratio for early anticoagulation in acute stroke.

Thus we share the careful considerations of the author toward the shortcomings and results of the existing studies on anticoagulation although we disagree with his conclusion: adapting to the risk of downhill skiing with modern technology combined with training resulted in both breathtaking records and a substantial reduction in the “complication” rate of this discipline. Similarly potential risks of anticoagulation should be minimized by appropriate selection and monitoring of patients treated with definitely more sophisticated protocols than are needed for standard aspirin recommendation. Recent therapy concepts both in the United States and Canada3,4 as well as our country surveyed in 33 dedicated stroke centers, mostly university hospitals,5 reflect a pathophysiologically driven, wide-spread careful use of anticoagulation in selected patients and the use of heparinoids for the prevention of deep vein thrombosis in most immobilized patients. In all patients individual therapy decisions are dynamically adapted by a quick stroke workup based on stroke etiology, size of the infarction, history of anticoagulation disorders, and actual bleeding risks from patient premorbidity, etc, which were all not considered in IST and CAST.

In our view the author’s conclusion to the many legitimate points of criticisms could better have resulted in formulation of timely study concepts stratifying risk and benefit of anticoagulant use in acute stroke by employing criteria such as time window, imaging criteria, and stroke etiology.

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