Intravenous tPA for acute stroke

To the editor:

We are encouraged that the *CJEM* Journal Club chose to address the use of tissue plasminogen activator (tPA) for the treatment of acute stroke in nonspecialist centres.[1] Dr. Rhine's review of the Cleveland area experience[2] is timely and relevant. The question is, can communtiy hospitals administer tPA and achieve outcomes comparable to those reported by the NINDS trial?[3] If not, should access to tPA be limited to specialist centres?

The best evidence comes from well-designed randomized controlled trials. These trials have been summarized in a recent Cochrane Collaboration systematic review,[4] which includes information on intravenous tPA use derived from over 2,500 patients in 7 randomized trials, including NINDS. The systematic review shows early hazard related to symptomatic intracranial hemorrhage, but an overall longer-term benefit in selected groups of patients treated within 3 hours of symptom onset. Unfortunately, none of these trials included patients randomized in nonspecialist, community hospital settings.

As Dr. Rhine indicated,[1] the evidence about tPA use in nonspecialist centres comes from nonrandomized comparisons. The Cleveland investigators[2] evaluated 3 treatment groups (patients treated with tPA, matched patients not treated with tPA, and all ischemic stroke patients) in 29 teaching and nonteaching hospitals. However, because of nonrandom allocation, these comparisons are subject to a number of biases, which may have caused the results to deviate significantly from the truth. In addition, only 70 (1.8%) of the Cleveland patients received tPA. This 1.8% treatment rate reflects other published figures, but the number of patients and adverse outcomes is small, therefore vulnerable to the play of chance. As interesting as the results are, they may not be accurate, and it is probably not reasonable to use them to suggest that tPA should be limited to tertiary care centres.

There is a need for further randomized comparisons. The Third International Stroke Trial (IST-3), now ongoing in the UK and Europe, is a large, well designed multicentre trial evaluating the use of tPA in patients with acute ischemic stroke. IST-3 is recruiting patients who present within a 6-hour time window from a wide variety of hospital settings, and will provide more valid data regarding the use of tPA in nonspecialist centres.

Tissue plasminogen activator is one small part of a "systems approach" to stroke treatment. More patients will benefit from stroke units and ASA because the vast majority of stroke victims are eligible for these, while only a small number currently receive tPA. Having said this, tPA has been the impetus for tremendous changes in stroke care, and it is anticipated that trials like IST-3 will help make tPA available to a larger number of people.

Finally, we disagree that subcutaneous heparin offers "similar benefits with less risk and lower cost." A recently published systematic review[5] suggests that the use of anticoagulants (including heparin) for the treatment of acute stroke results in no net improvement in long-term outcome, and increases the chance of fatal and nonfatal intracranial hemorrhage. In general, anticoagulants should be avoided in the management of the acute stroke patient.

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[Dr. Rhine responds:]

I agree with Drs. Gubitz and Phillips[1] that tPA is one small part of a "systems approach" to stroke treatment. I also agree that more patients will benefit from stroke units and ASA because the vast majority of stroke victims are eligible for these, while only a small number currently receive tPA. The importance of the Cleveland paper[2] is to emphasize that the risks of tPA may be higher in community hospitals than in research settings. I also intended to infer that, in community hospitals, stroke patients may benefit more from stroke teams, stroke units and other potentially less injurious interventions, such as ASA.

The CAEP Position Statement on "Thrombolytic Therapy for Acute Ischemic Stroke," published in this issue[3] of *CJEM*, agrees with my interpretation of the evidence and suggests that stroke thrombolysis should be limited to centres with rapid 24-hour access to specialized neurological expertise and neuro-imaging resources. Requirements suggested in the document, along with the currently recog-

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