Response to Letter by Longstreth and Tirschwell

Response:

We thank Drs Longstreth and Tirschwell for their comments on our article on off-label use of alteplase in stroke patients. Naturally, we did not reference their article on the National Institute of Neurological Disorders and Stroke (NINDS) trial patients older than 80 years because their article was published only after our final version was accepted. Unfortunately, their article adds little light to the question of thrombolysis in the octogenarians, because they do not report baseline characteristics when imbalances could easily explain differences with such small numbers of patients (19 placebo vs 25 alteplase). They also use an unclear definition for a symptomatic intracerebral hemorrhage, different from the several existing definitions, which makes their report difficult to compare with other data.

In our series of 1000 consecutive patients treated with intravenous alteplase in routine practice, 16% were older than 80 years. We found a trend toward excess symptomatic intracerebral hemorrhage with advanced age, which became nonsignificant in multivariate analysis, after potential confounders had been taken into account; the difference was mostly explained by baseline elevated glucose and early infarct signs. Our material even included 12 patients older than 90 years, of whom only 1 had a symptomatic intracerebral hemorrhage according to the European cooperative acute stroke study criteria, and 4 had a good outcome at 3 months (modified Rankin Scale score, 0–2), and similar results in the oldest patients have been reported elsewhere.

Irrespective of symptomatic intracerebral hemorrhage, older age and more severe baseline symptoms are the most important predictors of outcome in any stroke patient, and thus it is only natural that older patients fare worse than younger ones after thrombolysis. This also was the case in our cohort treated with ultra-early thrombolysis in which lower blood glucose level, younger age, lower baseline National Institutes of Health Stroke Scale, and onset-to-needle time <70 minutes were associated with better outcome. Although advanced age reduces the likelihood of good outcome, this does not mean that alteplase would cease to benefit stroke patients after a certain age. We think that with carefully streamlined services, thrombolytic therapy can benefit a fair portion of ischemic stroke patients, including octogenarians. In the year 2009, we treated 265 patients, 22% of our ischemic stroke patients, with alteplase, and over the past year we have achieved a median onset-to-needle time of 115 minutes and door-to-needle time of 20 minutes. We will continue to treat octogenarians with alteplase when otherwise indicated, just as do many other seasoned stroke services in Europe and elsewhere. Streamlined systems and well-trained teamwork may, in part, explain our better results compared with the patients in the NINDS trial. The pivotal trial opened the gates for thrombolysis in stroke 15 years ago, but many things have improved in stroke care since.

The Third International Stroke Trial aims to randomize ~1000 patients (www.dcn.ed.ac.uk/ist3) and the Italian TESPI trial 600 patients (www.strokecenter.org/trials) older than 80 years to intravenous alteplase vs placebo. These trials will increase our knowledge of alteplase safety and efficacy, specifically in the older patients, and the first results are awaited in spring of 2012. While waiting for these, we consider it unethical to withhold treatment based on patient’s age only.

Disclosures

A.M. received honoraria from Boehringer Ingelheim (modest). M.K. received honoraria from Boehringer Ingelheim, PAION AG, Forest Research Laboratories, and Lundbeck AS for participating in Steering Committee meetings of all ECASS and Desmoteplase in Acute Ischemic Stroke Trial (DIAS) trials (modest), and is a consultant for and on the Advisory Boards of Boehringer Ingelheim, PAION AG, Forest Research Laboratories, and Lundbeck AS (modest).

Atte Meretoja, MD, MSc (Stroke Med)
Markku Kaste, MD, PhD, FAHA, FESO
Department of Neurology
Helsinki University Central Hospital
Helsinki, Finland

Response to Letter by Longstreth and Tirschwell
Atte Meretoja and Markku Kaste

Stroke. 2010;41:e581; originally published online August 26, 2010;
doi: 10.1161/STROKEAHA.110.597732

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/41/10/e581

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/