**Editorial Comment**

**Efficacy and safety of single-bolus tenecteplase compared with front-loaded alteplase in Chinese patients with acute myocardial infarction**

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Following ST-segment elevation myocardial infarction (STEMI), early and complete epicardial reperfusion is associated with improved survival.1 For decades, the only available pharmacologic intervention aimed at reperfusion was intravenous streptokinase (SK). The efficacy of (SK) was firmly established in the Italian Group for the Study of Streptokinase in Myocardial Infarction (GISSI-1) trial, which reported an 18% relative reduction in mortality among patients presenting with STEMI within 12 hours after the onset of symptoms.2 Despite the fact that tissue-plasminogen activator (t-PA) is associated more rapid dissolution of thrombus,3 three large-scale clinical trials did not report a difference in mortality between SK and alteplase t-PA.4-6 It took altering the method of administration of alteplase t-PA, so-called front-loading (i.e. two-thirds of the dose over the first 30 minutes and the remaining dose over 60 minutes) rather than a 3-hour infusion, to lower mortality by about 1% with alteplase t-PA over SK.7 The drawback of alteplase t-PA was a small but significant increase in the risk of hemorrhagic stroke.

Attempts at improving mortality among patients with STEMI treated with fibrinolytic therapy have again met a roadblock. Genetic manipulation of alteplase t-PA has led to the production of t-PAs with longer half-lives, including reteplase t-PA and tenecteplase t-PA. Despite early promising results8 and a longer half-life and easier administration than alteplase t-PA,9 reteplase t-PA, given in a double-bolus fashion, did not improve outcomes when compared head-to-head in the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) trial.10

Tenecteplase t-PA, so-named because of the amino acid substitutions that make it different from alteplase t-PA, has a half-life about five times that of alteplase t-PA,11 making it even easier to administer. In the Assessment of the Safety of a New Thrombolytic (ASSENT-2) trial,12 tenecteplase t-PA given as a single bolus over 5-10 seconds had no significant effect on mortality when compared with alteplase t-PA in front-loaded fashion, but patients randomized to tenecteplase t-PA had significantly fewer non-cerebral hemorrhagic events and received fewer blood transfusions.

This apparent improvement in side effects coupled with the ease of administration of tenecteplase t-PA makes it an attractive option in multiple settings. The ASSENT-2 trial, however, was undertaken in countries in North America, South America, Europe and the Middle East. It has not yet been evaluated in the Asian population specifically. In this issue of *Journal of Geriatric Cardiology*, Liang et al. sought to evaluate the safety and efficacy of tenecteplase t-PA versus alteplase t-PA in Chinese patients.13

They randomized 110 patients, all of whom received aspirin and unfractionated heparin and underwent coronary angiography within 90 minutes to assess patency of the infarct-related artery. There were no significant differences in the rate of Thrombolysis in Myocardial Infarction (TIMI) Grade 3 flow, stroke, intracranial or any other hemorrhage, and overall mortality at 30 days. The rates of death (13.8% with tenecteplase t-PA, 9.6% with alteplase t-PA) were unexpectedly high, however, leading the authors to conclude that tenecteplase is not yet ready for general use among Chinese patients with STEMI who are to undergo fibrinolytic therapy.

There are multiple likely reasons for the difference in mortality among patients in the current trial when compared to other contemporary trials of patients with STEMI treated with fibrinolytic therapy, including ASSENT-2 (about 6%) and GUSTO (about 7%).10,12 Patients in the current trial were more likely to have had an anterior MI, more likely male, more likely to be smokers and were more likely to have a Killip class =2 than either of these other large-scale trials. In addition, patients who received tenecteplase t-PA were nearly significantly more likely to have a higher Killip class than those randomized to alteplase t-PA. The findings in the current study, therefore, should be interpreted with caution.

Large-scale international randomized trials have evaluated the safety and efficacy of tenecteplase t-PA in compar-
son with alteplase t-PA, and patients randomized to tenecteplase t-PA in those studies had similar ischemic outcomes with a lower risk of bleeding, one of the major drawbacks of alteplase t-PA. Another significant advantage of tenecteplase t-PA is its ease of single-bolus administration as opposed to two boluses 30 minutes apart with alteplase t-PA. That these authors were unable to document the previously established benefits of this pharmacologic advantage in a Chinese population may relate to the small sample size of the trial. While the current results do not warrant dismissal of alteplase t-PA in favor of tenecteplase t-PA, further larger studies are warranted in the Chinese population before firm conclusions regarding the safety and efficacy of tenecteplase t-PA can be made.

References