Thrombolytic Therapy in Morbidly Obese Patients

Key words: thrombolytic therapy, morbid obesity

In an ACCEL interview published in September 2003, Dr. Allan Ross and I discussed a patient with an acute anterior myocardial infarction (AMI) who was given the usual dose of thrombolytic therapy despite the fact that he weighed 290 pounds. The patient was transferred to a site where angioplasty could be performed, and, at the time of angioplasty, his ST segments were persistently elevated and his left anterior descending coronary artery was occluded. Perhaps the occlusion persisted because the dose of thrombolytic therapy was too small. This, of course, is speculation.

As we discussed this patient, I remembered a patient who arrived in our emergency department soon after onset of chest pain. An electrocardiogram revealed marked ST-segment elevation. Taking the patient to the catheterization lab was not an option since the patient weighed 450 pounds. Thrombolytic therapy was initiated by the emergency department physician and I was asked what dose would be appropriate in a patient of this weight. At the time, I recommended the accelerated regimen using 100 mg tissue plasminogen activator (tPA). I also contacted Genentech, Inc., for any information about the use of thrombolytic therapy in grossly obese patients having an acute ST-segment elevation MI. Genentech did not recommend exceeding the approved maximum dose, regardless of patient weight, because of the increased risk of intracranial bleeding.

Now, admittedly, this has got to be a rare event, that is, AMI in a 450-pound person, but it does pose the interesting question of how a morbidly obese patient who is not eligible for acute angioplasty should be dosed.

Over the past several years, several articles have been written about weight-adjusted dosing of thrombolytic therapy, but most of these focus on reducing the incidence of bleeding at the lower body weights. An inverse relationship between body weight and intracranial hemorrhage has been observed on many occasions, that is, lower body weight, higher incidence of intracranial bleeding, despite weight-adjusted dosing.

In an effort to bring myself and the readers of this editorial up to date on the use of thrombolytic therapy in grossly obese patients, I contacted Genentech and received the following information: the recommended total dose should not exceed 50 mg and is based upon patient weight. Nothing was mentioned about doses in morbidly obese patients.

A Medline search uncovered one article that I will summarize for the reader. Angeja et al. used a weight-adjusted dose of tenecteplase (TNK) to treat AMI. For patients < 60 kg, a dose of 30 mg TNK was used. For every 10-kg increase up to 90 kg, the dose of TNK was increased by 5 mg. Thus, at ≥ 90 kg, 50 mg TNK was given. Nothing has been reported about patients in the morbid obese range.

In this study, patients weighing < 60 kg had a higher 30-day mortality and an increased incidence of intracerebral hemorrhage, despite weight adjustment, compared with patients ≥ 90 kg receiving weight-adjusted doses of TNK with gradients from 60 to 90 kg decreasing for both mortality and intracranial hemorrhage.

If one does a straight-line extrapolation of a dose of TNK adjusted for body weight from 60 kg to 100 kg as was done in the above clinical trial, then, theoretically, the dose of TNK should be 100 mg for a 200 kg patient (using a 5-mg increase for every 10 kg of body weight). Obviously, at this dose range, the concern would be for an increased incidence of intracerebral hemorrhage, but as far as I can tell there are no data available to help guide the clinician in this unusual circumstance.

Summary

Most of the concern about dosing thrombolytic agents as presented in the literature is related to the lower weight groups and the increased incidence of bleeding in this patient population. Not much is known or written about what dose of thrombolytic therapy should be used in the grossly obese patient with an AMI. Although it may be uncommon to have a morbidly obese patient with an AMI, it does occur. Perhaps body weight doesn’t matter since we are really dosing the clot and not the body, but, as far as I can discern, there are no data regarding dosing of thrombolytic drugs to guide the clinician managing these patients.

C. Richard Conti, M.D., M.A.C.C.
Editor-in-Chief

References