Platelet inhibitor reduces size of large heart attacks

March 26 2012

The anti-platelet drug abciximab, delivered directly to lesions caused by a heart attack, significantly decreased damage to the heart muscle in high-risk patients while clot aspiration showed no impact, according to research presented today at the American College of Cardiology's 61st Annual Scientific Session. The Scientific Session, the premier cardiovascular medical meeting, brings cardiovascular professionals together to further advances in the field.

Angioplasty is performed during a heart attack to restore blood flow and reduce the size of the infarct – permanent damage to the heart muscle – which begins within minutes after the onset of chest pain and can continue for up to 12 hours. Too often, however, heart damage is extensive. In some cases the culprits are distal emboli, plaque or blot clots that break off during angioplasty and lodge in smaller vessels, essentially moving the heart attack downstream to smaller arteries.

Two approaches to prevent this process have been studied extensively with highly conflicting results: (1) delivering high concentrations of abciximab to the blood clot (thrombus) at the site of the lesion, where it keeps platelets from sticking together and causes the clot to collapse, and (2) sucking out the clot through a process called manual aspiration thrombectomy.

"All of the earlier studies have limitations," said Gregg W. Stone, MD, director of cardiovascular research and education, Columbia University Medical Center/New York-Presbyterian Hospital, New York City, and

principal investigator of the INFUSE-AMI trial. "To clarify which approach, if any, can reduce the size of the heart attack, we studied only patients presenting within four hours of symptom onset with a large anterior heart attack, with blockage of the largest heart artery confirmed by cath lab. These are destined to be very large heart attacks, but the patients presented early enough for us to be able to reduce the amount of damage."

INFUSE-AMI used a 2 x 2 factorial design, which isolates the impact of each intervention to maximize the chance of identifying any reduction in heart attack size. The trial, conducted at 37 sites in six countries, screened 6,318 patients and enrolled 452 (7.2 percent). It is a single-blind study in which the operator knew the randomization assignments.

Participants were randomly assigned to one of four arms: (1) aspiration plus abciximab; (2) aspiration without abciximab; (3) no aspiration plus abciximab; and (4) no aspiration or abciximab (control). In the two abciximab arms, a "weeping" balloon catheter delivered the drug right to the site of the lesion, which "invariably has a thrombus," Dr. Stone noted. A catheter was used to aspirate clots. All patients who had angioplasty were given bivalirudin, an anticoagulant that keeps bleeding and mortality low.

The primary efficacy endpoint was heart attack size at 30 days, as measured by cardiac MRI for 382 of 439 surviving patients (87.1 percent). Heart attack size was gauged by calculating infarct size as a percentage of total heart muscle tissue. Patients in the two abciximab arms had significantly smaller heart attacks than patients in the two no-abciximab arms (median 15.1 percent vs. 17.9 percent). By contrast, aspiration thrombectomy did not decrease heart attack size (17.0 percent) compared with no aspiration (17.3 percent). The aspiration plus abciximab group showed the lowest median heart attack size of 14.7 percent, compared with 17.6 percent for the other three groups

combined. Clinically, there were no significant differences among the four groups for any major measures of safety or efficacy at 30 days. Patients will be assessed again at six months and one year.

"This study is important because it demonstrates that in patients with large heart attacks who reach the hospital early, we can reduce the magnitude of heart damage with a bolus of intracoronary abciximab delivered directly to the infarct lesion," Dr. Stone said. "The next step is a larger randomized clinical trial of the two arms of our study that did reduce heart attack size, to determine whether this therapy results in an important clinical benefit, as one might expect."

Atrium Medical, manufacturer of the ClearWay RX catheter, funded and participated in design of the study. Dr. Stone serves as a consultant to Atrium Medical and to Medtronic, which manufactures the Export aspiration catheter used in the study, to Eli Lilly, distributor of abciximab, and to The Medicines Company, maker of bivalirudin.

This study will be simultaneously published in the *Journal of the American Medical Association.*

Provided by American College of Cardiology