Facilitated PCI Fails in Multicenter FINESSE Trial

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VIENNA — The once-promising concept of pharmacologically facilitated percutaneous coronary intervention for patients with ST-elevation MI now appears relegated to the scrap heap on the basis of the negative results of the large definitive Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events (FINESSE) trial.

"In terms of using [facilitated PCI] as part of a broad approach for patients, I think it's dead," FINESSE coprincipal investigator Dr. Stephen Ellis said at the annual congress of the European Society of Cardiology.

Primary PCI has been shown to be superior to thrombolytic therapy as a revascularization strategy for most patients with STEMI, but delays in getting to the cath lab are common, particularly when transfer to another hospital is required. The hypothesis underlying facilitated PCI was that when a delay of an hour or more was anticipated, improved clinical outcomes would be achieved by opening the infarct-related artery early with a thrombolytic agent and/or glycoprotein IIb/IIIa inhibitor while waiting for PCI. FINESSE, the largest-ever facilitated PCI trial, showed that's not the case, said Dr. Ellis of the Cleveland Clinic Foundation.

FINESSE involved 2,453 patients in 20 countries who presented with STEMI within 6 hours of chest pain onset and had an anticipated 1- to 4-hour delay to cardiac catheterization for primary PCI. They were randomized to one of two facilitated PCI strategies or to primary PCI with abciximab administered in the cath lab. The facilitated PCI approaches studied were half-dose reteplase plus abciximab, or abciximab alone. Average door-to-balloon time was 2.2 hours.

The primary end point was a 90-day composite of all-cause mortality, rehospitalization or treatment of heart failure in the emergency department, cardiogenic shock, or resuscitated ventricular fibrillation occurring more than 48 hours post randomization. The rate was 10.7% with primary PCI, 10.5% with abciximab-facilitated PCI, and 9.8% with combined facilitation, a nonsignificant difference.

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Moreover, there was a downside to the facilitated PCI approaches. Major bleeding occurred in 4.8% of patients with combined facilitation, 4.1% with abciximab facilitation, and 2.6% with primary PCI. The combined rate of TIMI major or minor bleeding was 14.5% with dual reteplase/abciximab-facilitated PCI, 10.1% with abciximab-facilitated PCI, and 6.9% with primary PCI. There was also a strong albeit nonsignificant trend for more intracranial hemorrhages in the combined facilitation group.

Discussant Dr. Frans Van de Werf said one explanation for the negative results was the use of suboptimal antithrombotic cotherapy. FINESSE, he noted, didn't require enoxaparin or up-front clopidogrel because the trial was designed prior to publication of persuasive evidence of the importance of these therapies in STEMI patients.

He added that FINESSE may also have been doomed because it studied the wrong population, since it enrolled patients presenting up to 6 hours after symptom onset. "It's clear that in patients presenting after 3-4 hours there's little to gain by a slightly higher patency rate achieved by giving pharmacological therapy," asserted Dr. Van der Werf, professor and chairman of the department of cardiology at University Hospital Gasthuisberg, Leuven, Belgium.

While he concurred with Dr. Ellis that facilitated PCI using the strategy tested in FINESSE can't be recommended, Dr. Van de Werf also announced that a variant approach will be put to the test in a large randomized trial called to begin early next year. (See sidebar below.)

FINESSE was funded by Centocor and Eli Lilly. ■

'Pharmacoinvasive' Strategy in STEMI

A reinvigorated role for thrombolytic therapy in ST-elevation MI as an alternative to primary percutaneous coronary intervention will be studied in a 2,000-patient randomized multicenter trial to begin early next year, Dr. Van de Werf said.

The STREAM (Strategic Reperfusion Early After Myocardial infarction) trial will test what he termed a "pharmacoinvasive strategy" involving prehospital administration of tenecteplase to STEMI patients presenting within 3 hours of symptom onset and having an anticipated lengthy delay to PCI.

Unlike the facilitated PCI strategy, which has fallen by the wayside in the wake of the negative FINESSE trial, the pharmacoinvasive strategy restricts immediate PCI to those patients who don't demonstrate at least 50% ST-segment resolution in response to lytic therapy. In those who do show evidence of successful reperfusion after prehospital lytic therapy, cardiac catheterization will be postponed for up to 24 hours, explained Dr. Van de Werf, principal investigator in STREAM.

The STREAM hypothesis is that prehospital lysis provides outcomes as good as or better than primary PCI in patients presenting early with STEMI. Participants will receive state-of-the-art antithrombotic therapy with up-front clopidogrel and enoxaparin rather than unfractionated heparin in accord with the results of the Clopidogrel as Adjunctive Reperfusion Therapy–Thrombosis In MI 28 (CLARITY-TIMI 28) and Enoxaparin and Thrombosis Reperfusion for Acute Myocardial Infarction Treatment–Thrombosis In Myocardial Infarction 25 (EXTRACT-TIMI 25) trials, added Dr. Van de Werf.

STREAM is sponsored by Boehringer Ingelheim.

CARESS: Immediate Transfer for PCI Best After Successful Lysis

VIENNA — Immediate transfer for percutaneous coronary intervention after successful thrombolytic therapy in patients with ST-elevation MI provides markedly better outcomes than does a more conventional strategy of continued medical treatment in the non-PCI hospital, with transfer for rescue PCI only in the event of continued ST elevation at 90 minutes, Dr. Carlo Di Mario reported at the annual congress of the European Society of Cardiology.

This was the key finding of the Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction (CARESS in AMI). The three-country European trial compared two strategies for managing ST-segment elevation myocardial infarction (STEMI) patients for whom the preferred treatment—primary PCI—is anticipated to be unavailable within 90 minutes of their presentation at a non-PCI hospital.

CARESS involved 600 such patients who received half-dose reteplase, abciximab, aspirin, and unfractionated heparin. They were then randomized to immediate transfer for PCI or to transfer for rescue PCI only in the event of continued ST elevation at 90 minutes, which occurred in 36% of patients assigned to that study arm, explained Dr. Di Mario of Royal Brompton Hospital, London.

The primary study end point was a composite of death, repeat MI, or refractory ischemia at 30 days. The rate was 4.1% in the immediate transfer/PCI-for-all group, compared with 11.1% in the rescue PCI group. That's a 63% relative risk reduction in favor of the immediate-transfer strategy, noted Dr. Di Mario, a CARESS coprincipal investigator.

Patients averaged 170 minutes from onset of chest pain to reteplase. The median time from reteplase to PCI was 136 minutes in the immediate transfer group and 212 minutes in the rescue PCI patients.

Although the rate of any bleeding was significantly increased in the immediate transfer/PCI-for-all group—12.2% compared with 7.4%—severe bleeding and intracranial hemorrhages were rare and not significantly different between the two study arms.

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"I believe this was due to the exclusion of patients at high risk of bleeding," he commented. "This is a strategy for patients under 75 years old who have high-risk MIs and a low risk of bleeding."

Indeed, the mean age of study participants was just 60 years.

Discussant Dr. Freek W.A. Verheugt noted that CARESS is the fourth study to show that STEMI patients should routinely undergo early PCI following successful lytic therapy. All four trials were small to moderate in size.

Where do things stand with respect to STEMI management in 2007 in light of CARESS and other recent studies? If PCI can be performed by experienced operators within 90 minutes of patient presentation, the treatment of choice is clearly primary PCI. If primary PCI within 90 minutes isn't available, a lytic should be given. If it doesn't accomplish reperfusion, urgent transfer for rescue PCI is warranted, said Dr. Verheugt, professor and chairman of the department of cardiology at University Hospital, Nijmegen, the Netherlands.

Even if there is reperfusion, however, PCI is still clearly necessary as shown in CARESS and three other trials. The key question is, when should it be done? That's unresolved. CARESS showed excellent outcomes with an average interval between lytic therapy and PCI of about 2¼ hours. That brief an interval could be tough to duplicate in clinical practice, especially for patients who present to hospitals in remote areas. At the other extreme, the Spanish GRACIA-1 trial showed similar benefits with a 17-hour interval, which is a lot more convenient for patients, transport crews, and cath lab personnel than a rushed dead-of-night transfer, he continued.

"We need a randomized trial of early versus late transport for auxiliary PCI in patients who are reperfused and stable after lytic therapy," Dr. Verheugt concluded.

CARESS was sponsored by the Italian Society of Interventional Cardiology, with grants from Eli Lilly & Co. and Biotronik AG. ■