Early Intervention Beneficial for ACS Patients

BY CAROLINE HELWICK

NEW ORLEANS — In patients with non–ST-segment elevation acute coronary syndromes, invasive treatment within 24 hours causes no harm, and in high-risk patients it may reduce the risk of adverse cardiovascular events, compared with delaying intervention, according to results of a large international trial.

The Timing of Intervention in Acute Coronary Syndrome (TIMACS) trial, involving 3,031 patients treated at 100 medical centers in 17 countries, "is the largest trial there will ever be on this topic. It is immediately relevant to patients, doctors, and the health care system," said Dr. Deepak Bhatt, the study's discussant at the annual scientific sessions of the American Heart Association.

TIMACS compared the relative usefulness, safety, and cost-effectiveness of early angiography (within 24 hours), followed by revascularization if necessary, with procedures delayed more than 36 hours after the onset of unstable angina or non-ST-segment elevation myocardial infarction (NSTEMI). Eligible patients were treated with aspirin, clopidogrel, and/or a glycoprotein IIb/IIIa antagonist in accordance with routine practice and were then randomized to receive either early or delayed intervention.

"We have very good data in patients with myocardial infarction that timely thrombolytic therapy is of utmost importance," the principal author, Shamir R. Mehta, said in describing the rationale for the study. "But we have less information on the importance of timing in patients with unstable angina, threatened MI, or NSTEMI."

For the primary end point, a composite of death, recurrent MI, or stroke within 6 months, the study found no significant risk reduction in favor of early intervention: 9.7% occurred in the early intervention group, compared with 11.4% in the delayed group, for a 15% relative reduction in risk that did not reach statistical significance, reported Dr. Mehta, director of interventional cardiology at Hamilton (Ont.) Health Sciences.

However, for several secondary outcome measures, differences favored early intervention. These included the composite of death, MI, and refractory ischemia, with rates of 13.1% in the delayed arm and 9.6% with early intervention; the composite of death, MI, stroke, refractory ischemia and repeat intervention, which occurred in 19.7% and 16.7%, respectively; and the outcome of repeat interventions, which occurred in 8.8% and 8.6%, respectively.

But it was the patients considered to be at the highest risk who benefited most from early intervention. Striking differences emerged when patients were stratified by the Global Registry of Acute Coronary Events (GRACE) risk score. Early diagnostic angiography reduced the relative risk of the composite end point of death, repeat MI, or stroke by 35% in a high-risk subset of patients with NSTEMI. For patients with low or intermediate risk for death with acute coronary syndromes (about two-thirds of the cohort), the slower strategy was just as effective, reported Dr. Mehta, also of McMaster University, Hamilton, Ont.

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DR. MEHTA

For patients with a high GRACE score (at least 140), the rate of death, MI, or stroke at 6 months was 21.6% with delayed intervention, compared with 14.1% with early treatment, a significant difference. In the low- to intermediate-risk group, the difference between the strategies was not statistically significant, at 6.7% and 7.7%, respectively.

"In the highest risk subset, early intervention appeared superior, and these patients should be taken to the cath lab as soon as possible. With others, the timing depends on additional factors. Since there are no safety concerns with early intervention, and given that it lowers refractory ischemia by about 70%, it is a reasonable routine option for all patients with ACS," Dr. Mehta concluded.

"There has been a concern that it may be dangerous to take patients with these forms of chest pain to the catheterization lab too quickly, that a period of 'cooling off' with medical therapy may be of benefit. This has been disproved. There is no detriment to going early and there is definitely a shorter hospital stay. In high-risk patients, this trial proves there is clearly a benefit to early intervention, which is consistent with clinical common sense," said Dr. Bhatt, chief of cardiology at the VA Boston Health Care System and director of the Integrated Interventional Cardiovascular Program at Brigham and Women's Hospital, Boston. ■

Adult Congenital Heart Disease Costs

NEW ORLEANS — The annual number of hospitalizations for adults with congenital heart disease climbed by 71% in the United States between 1998 and 2005, far outstripping the 12% overall increase in hospital admissions among the general adult population.

Total hospital charges for adults with congenital heart disease (ACHD) skyrocketed from $1.1 billion in 1998 to $3.7 billion in 2005, a disproportionate increase relative to trends in the broader adult population. Indeed, this 229% jump in total charges was more than twice the rate of increase for all adult hospitalizations nationally during the same period, Dr. Alexander R. Opotowsky noted at the annual scientific sessions of the American Heart Association.

His analysis of data from the Hospital Cost and Utilization Project's Nationwide Inpatient Survey, the country's largest all-payer hospital discharge database, provided a first-ever look at national hospitalization trends for the growing ACHD population.

Hospitalizations for complex forms of ACHD rose by 58% during the study period, while admissions for simple diagnoses climbed by 129%, driven largely by a sharp increase in admissions for patients with secundum atrial septal defect or patent foramen ovale, said Dr. Opotowsky of the University of Pennsylvania, Philadelphia.

Surgical as well as medical admissions increased. Patients with simple forms of ACHD were slightly more likely than those with complex diagnoses to be admitted for surgery, mainly to address bicuspid aortic valves and aortic insufficiency, he continued.

The annual number of hospitalizations for ACHD patients aged 55 or older increased by 78% between 1998 and 2005. The increase was 63% among 18- to 34-year-olds with ACHD and 67% in 35- to 54-year-olds.

"We now have an older, sicker population requiring more repeat admissions," the cardiologist said.

—Bruce Jancin

Computerized Test Predicted Acute Coronary Syndrome in the ED

BY PATRICE WENDLING

CHICAGO — A computerized pretest probability device accurately predicted acute coronary syndrome in low-risk chest pain patients and significantly reduced unneeded exposure to thoracic imaging as well as return visits to the emergency department in a randomized controlled trial of 400 patients.

The Web-based software device (PRETestConsultACS) produces a point estimate of ACS based on eight predictor variables: age, sex, race, history of coronary artery disease, chest wall tenderness to palpation that reproduces chest pain, diaphoresis, ST depression greater than 0.5 mm in two leads, and T-wave inversion greater than 0.5 mm in two leads.

The variables are entered into a personal computer or personal digital assistant that searches a large database for evaluated patients who share the same profile. The percentage of matched patients who have ACS equals the pretest probability. ACS included myocardial infarction; coronary stenosis greater than 60% prompting new medical management or revascularization; ventricular arrhythmia; cardiogenic shock; or bradycardia requiring therapeutic intervention.

After obtaining a clinician's estimate of pretest probability of an ACS, 400 patients (mean age, 46 years) and their emergency clinicians were randomized to receive a written printout from the computer, or not. In all, 31 patients were excluded.

Pretest probability estimates of an ACS generated by the emergency clinician (mean, 4) correlated significantly with estimates from the software device (mean, 4), according to a poster at the annual meeting of the American College of Emergency Physicians.

A significant cardiovascular diagnosis was made in 36 (19.4%) of the 185 controls and 35 (19%) of the 184 intervention-group patients.

Researchers discovered one case of a missed or delayed diagnosis of ACS within 45 days, the study's primary safety end point, in a control-group patient, said lead investigator Dr. Jeffrey Kline and his colleagues in the department of emergency medicine, Carolinas Medical Center, Charlotte, N.C. The patient was diagnosed with unstable angina that was treated with a percutaneous intracoronary stent device 21 days after enrollment.

The rate of hospital admission of patients who had no significant cardiovascular diagnosis within 45 days was significantly higher among controls (11%) than in the intervention group (5%).

The rate of exposure to a thoracic imaging test that imparted greater than 5 mSv and had a negative result was significantly greater among controls (19.4%) than in the intervention group (8.6%). The lifetime risk of malignancy is thought to increase significantly after a dose of radiation that exceeds 5 mSv.

"If the results of this study are independently validated in a larger and different sample of patients, then clinicians will have evidence to justify the use of quantitative pretest probability, together with their own clinical instincts, to reduce excessive diagnostic testing in low-risk patients with chest pain," Dr. Kline said in an interview.

Median length of stay in the emergency department was not significantly different between the control (11.4 hours) and intervention (9.2 hours) groups.

Based on telephone follow-up, patients in the intervention group were less likely than were those in the control group to be readmitted within 7 days of their emergency visit (4% vs. 11%), according to the investigators, who reported no relevant conflicts. ■