Other News

Challenges In Acs

Biomarkers and Diagnosis

"We need to be cautious about 'cookbook' approaches that do not account for individual patient variations," said James DeLemos, MD, Associate Professor, University of Texas Southwestern Medical Center, Dallas, acknowledging that patient variations can be difficult to appreciate on clinical grounds alone (e.g., history, PE, ECG); which makes biomarkers all the more important.

"The prototype cardiac biomarkers are the troponins (cTnT, CTnI). These are powerful prognostic markers that can help confirm MI—but they're also associated with pulmonary embolus (PE), heart failure, and sepsis."

In addition to identifying patients in the midst of an event and/or at high risk, troponins are associated with active thrombotic processes. Dr. DeLemos identified troponins as "optimum biomarkers" and went on to present results from several studies demonstrating that treatment with enoxaparin, and the GP IIb/IIIa inhibitors, and an invasive approach to revascularization significantly reduce event rates in troponin-positive patients.

Dr. DeLemos discussed emerging cardiac biomarkers, including myeloperoxidase and brain natriuetic peptide (BNP). Myeloperoxidase, however, is also a marker for autoimmune diseases and cancer. And BNP elevations are also seen in right ventricular overload states.

"The new biomarkers are promising," Dr. DeLemos said, "but there remains a tremendous need for even more specific cardiac biomarkers."

Modifying Thrombosis

Deepak Bhatt, MD, Department of Cardiovascular Medicine, Cleveland Clinic, echoed the importance of troponin links to thrombosis. Dr. Bhatt discussed the implications of several key studies, notably the SYNERGY trial (*JAMA* 2004;292:45-54) which supported the use of the low molecular weight heparin enoxaparin over unfractionated heparin. In this study, enoxaparin was not found to be absolutely superior.

Dr. Bhatt noted that enoxaparin was an adequate "noninferior" alternative for the treatment of high-risk patients with NSTEMI ACS. "The endorsement is there, but it is not resounding," he said.

Overall, most of the recent research consistently supports antithrombotic therapies as a cornerstone of early treatment in ACS—along with moving quickly to invasive strategies. "Early invasive intervention in NSTEMI ACS is preferred," Dr. Bhatt said. "The data supports that this is where we reduce mortality and improve outcomes."

Dr. Bhatt called for additional research to develop more and better antithrombotic agents. "The optimal drug timing and combination is yet to be determined in managing thrombotic complications in ACS," he said.

Assessing and Modifying Inflammation

Mary Cushman, MD, Associate Professor of Medicine (Hematology/Oncology), University of Vermont School of Medicine, Burlington, stated that elevated levels of C-reactive protein (CRP)—even in asymptomatic individuals—are associated with an up to four-fold increase in CVD risk.

"CRP rises in ACS and is higher in those with cardiovascular disease in general," said Dr. Cushman, who also highlighted that CPR is produced in smooth muscle cells within human coronary arteries and is expressed preferentially in diseased coronary vessels.

The data is "very substantive," Dr. Cushman said, in support of CRP's role as an independent predictor of risk. "Many studies demonstrate that CRP is a surprisingly accurate predictor for stroke, MI, and peripheral arterial disease."

While this marker cannot be considered absolutely specific, Dr. Cushman said, "CRP rarely suggests other non-cardiac concerns." She cited studies in which CRP has been demonstrated to increase predictive value "at all levels of

LDL and at all levels of risk scoring." (However, Dr. Cushman said, CRP levels do not directly correlate with lipid measures, and simultaneous assays of CRP + lipids will add value to risk assessment and stratification.)

"What we're really talking about here, though, is reducing inflammation in our patients at risk," Dr. Cushman said. "And that brings us back to the fundamentals: lifestyle modification, weight loss, exercise. We need to see more and better control of blood pressure and impaired glucose tolerance. It's great to have biomarkers to guide us, but we have to control the multiple modifiable risks that patients face."

Revascularization Issues

Controversy has reigned regarding the merits of invasive versus conservative approaches to patients with ACS. Peter B. Berger, MD, Director of Interventional Cardiology, Duke University, Durham, NC, discussed several trials evaluating this question.

The ISAR-COOL study tested the hypothesis that unstable ACS patients might do equally as well if "bathed in" antithrombotics for a "cooling-off period" prior to revascularization. However, those patients delaying intervention for the antithrombotic pretreatment period did not see improved outcomes compared with "immediate intervention accompanied by intense anticoagulation," according to Dr. Berger.

On the other hand, the ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes) Trial (deWinter RJ et al, *N Engl J Med* 2005:353) found no difference in outcomes between early PCI and conservative approaches. One study arm consisted of troponin-positive patients randomized between early PCI or conservative (medical) treatment. Troponin-normal patients formed the control group. Primary combined endpoint was ACS, MI, or death.

ACC/AHA guidelines recommend that high-risk ACS patients benefit more from an early invasive strategy. Dr. Berger agreed, although conflicting data suggests a need for additional risk stratification guidelines to further identify ACS patients more likely to benefit from early interventions.

Early Initiation of Eptifibatide for Heart-Attack Patients in Emergency Department Achieved Superior Coronary Artery Blood Flow

A new study presented at an AHA Satellite Symposium hosted by the Texas Heart Institute announced that results from the Time to Integrilin Therapy in Acute Myocardial Infarction -Thrombolysis In Myocardial Infarction (TITAN-TIMI-34) study, indicated that the early initiation of eptifibatide in the emergency department prior to percutaneous coronary intervention (PCI) for acute ST-segment-elevation myocardial infarction (STEMI) yielded superior coronary artery blood flow, as assessed by TIMI frame counts, the study's primary endpoint. Also, superior myocardial perfusion, as assessed by TIMI myocardial perfusion grade, was found by early initiation of eptifibatide, compared to administration of eptifibatide in the cardiac catheterization laboratory after angiography. Bleeding and transfusions were the same in both groups.

"The longer a patient has poor blood flow to the heart, the higher the risk of cardiovascular damage," said C. Michael Gibson, MD, Brigham and Women's Hospital and principal investigator in the TITAN-TIMI-34 study. "Since delays in restoring blood flow via angioplasty are frequent, this trial demonstrated that the strategy of early intervention in the emergency department with eptifibatide improved blood flow prior to angioplasty."

Eptifibatide is approved for use in ACS (UA/NSTEMI), and patients undergoing PCI, but is not approved for use in STEMI patients not undergoing PCI.