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MYELOPEROXIDASE: A NOVEL ADDITION TO MULTIMARKER TESTING IN ACUTE CORONARY SYNDROMES

Of the 5.4 million people who present to emergency departments with chest pain each year (*1*), approximately 1.7 million have acute coronary syndromes (ACS) (*2*). Between 2% to 5% of those patients who are discharged will have unrecognized acute MI, and 25% of those patients will die (*3*). Current biomarkers used for identifying patients at high risk of ACS primarily include biomarkers of myocardial necrosis (troponin, CK-MB, myoglobin), or ischemia and myocardial stretch (BNP). Because these markers don't always identify high-risk patients, additional novel biomarkers are under investigation, including inflammatory cytokines, cellular adhesion molecules, acute-phase reactants, and plaque destabilization and rupture markers.

Myeloperoxidase Is an Early Indicator of Unstable Plaque

Myeloperoxidase (MPO) is an early marker of vulnerable plaque that elevates within 2 hours of the onset of symptoms (*4, 5*). Elevated levels suggest acute inflammation in the coronary circulation, due to increased neutrophil and monocyte activation, typically preceding myocardial injury (*5*). MPO also is enriched within culprit lesions prone to rupture or cause intracoronary thromboses in patients with sudden cardiac death (*2*). MPO level rises before other markers of cardiac necrosis and traditional markers, and has strong prognostic ability in patients presenting with chest pain and suspected ACS (*6*). MPO is especially useful in the troponin-negative patient, and provides the best detection of patients with the greatest risk when used as part of a multi-marker strategy with other markers, such as BNP, CK-MB, TNI and Myoglobin (*3*).

Stanley L. Hazen, MD, PhD, Section Head, Preventive Cardiology and Cardiac Rehabilitation at the Cleveland Clinic Foundation (Cleveland, OH), stated, "In patients presenting with a history of chest pain, such as in the emergency department or cardiology office, MPO can be used to help rapidly triage patients at high risk versus lower risk. A large number of patients have negative first troponin levels. Still more have persistently negative troponin levels, yet still are at increased risk for a major adverse cardiac event. An elevated initial MPO level helps rapidly identify subjects at increased risk of an MI, the need for bypass surgery, or dying within the next 6 months. When MPO levels are within the normal range, the risk of having one of those adverse cardiac events in the next 6 months is very low," he added.

Studies Show the Effectiveness of MPO

Researchers investigated the prognostic value of elevated serum MPO using the database of 1090 patients from the CAPTURE trial (*4*). The endpoints were death and MI during 6 months of follow-up. The study showed that elevated MPO predicts increased short- and long-term risk of MI and death, with statistical significance ($p < 0.001$). When MPO is compared with other markers, including TnT, sCD4OL, and CRP, MPO remained an independent predictor of increased risk at 30 days and 6 months. Patients with low TnT levels, yet high MPO levels, were still observed to be at increased risk ($p = 0.001$). The researchers concluded that MPO is a powerful predictor of adverse outcome in patients with ACS. Importantly, MPO identified patients with low TnT levels who were at increased risk for future cardiovascular events.

Another study found that a single initial measurement of MPO is an independent predictor of the early risk of MI and major adverse cardiac events in the following 30-day and 6-month periods (*5*). Brennan *et al*. assessed the MPO levels in 604 patients presenting sequentially to the emergency department with chest pain. Elevated initial MPO predicted the risk of MI, even for patients with negative troponin levels (< 0.1 ng/ml) at baseline ($p < 0.001$). The researchers

found that elevated MPO levels also predicted the risk of MI, the need for revascularization, or death within 30 days and 6 months of presentation ($p < 0.001$). Elevated MPO was predictive of increased risk, regardless of ECG findings, history of coronary artery disease, and levels of CRP, troponin, and CK-MB. They concluded that MPO has potential utility for risk stratification for patients presenting with chest pain, since it is the only marker that identified patients at risk for cardiac events in the absence of myocardial necrosis.

Multiple Markers Strategy is Needed for ACS

No single marker currently provides optimal specificity and sensitivity for the assessment of ACS, but the multiple marker strategy, including MPO, is important for risk stratification of patients with chest pain or suspected ACS. Baseline MPO levels are especially useful in predicting risk for patients with negative troponin levels. When used with other markers for ACS, MPO provides unique information to assist in assessement of patients at greatest risk of an adverse cardiac event.

Researchers in Germany studied MPO as an early indicator of ACS and a predictor of future cardiovascular events. They assessed the value of the leukocyte enzyme MPO for early diagnosis of ACS and for long-term risk of cardiovascular events (*6*). Blood samples from 1671 individuals with chest pain and from 262 control participants were analyzed for plasma MPO, troponin I, creatine kinase isoform MB, B-type natriuretic peptide, myoglobin, and C-reactive protein. The researchers found that plasma MPO levels rose immediately after the onset of chest pain and peaked in patients who presented within 0 and 3 hours of the onset of pain (57.1 ng/mL versus 7.6 ng/mL for the control participants, $P < .001$). For those presenting within 0 to 6 hours of the onset of pain, the area under the receiver-operating-characteristic curve for diagnosis of ACS was highest for MPO (0.87, 95% CI, 0.81 to 0.94) as compared to the established biomarkers, regardless of ST or non-ST elevation myocardial infarction or unstable angina. An increase in one standard deviation of MPO was associated with a 1.30-fold (95% CI, 1.12 to 1.49, $P < .001$) increase in adverse cardiovascular events within 30 days and remained unchanged after a mean of 2.5 years in a fully adjusted model. The study showed that single baseline MPO measurement is superior to the established biomarkers in the early diagnosis of ACS and that this marker is an independent predictor of short-and long-term cardiovascular risk.

To request additional information, please contact medicalaffairs@biosite.com. Educational materials will also be available at the Biosite booth, #823 and at the educational dinner program (information follows).

Biosite cordially invites you to participate in our complimentary educational program and dinner. Learn more about exciting developments using biomarkers and multi-marker testing in Acute Coronary Syndrome and Congestive Heart Failure. Wednesday, July 26, 2006 at Spiaggia Restaurant. 980 North Michigan Avenue, level 2(One Magnificent Mile Building), Chicago, Illinois 60611, 1-312-280-2750. Please RSVP to dinner@biosite.com or fax to 1-858 695-3823.

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