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Acute Coronary Syndromes

Novel Serum Markers for Risk Prediction in Acute Coronary Syndromes

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One of the most difficult problems in medicine is evaluating the patient who presents with chest pain. Among the myriad causes of chest pain are benign conditions such as costochondritis, serious but not life-threatening conditions such as pericarditis, and the truly life-threatening situations, such as acute coronary syndromes. Differentiating among these pathologies is sometimes quite difficult; thus new methods to separate the benign from the life threatening are being sought. It is increasingly recognized that atherosclerosis is an inflammatory disease.[1] Chronic, subclinical inflammation appears to be one mechanism leading to atherosclerotic plaque rupture and acute coronary syndromes. If, indeed, inflammation underlies acute coronary syndromes, then inflammatory molecules should be elevated in patients in the midst of acute coronary syndromes. Two recent papers address this phenomenon and are reviewed below.

Prognostic Value of Myeloperoxidase in Patients with Chest Pain

Brennan ML, Penn MS, Van Lente F, et al.
N Engl J Med. 2003;349:1595-1604.

Myeloperoxidase is an enzyme released by inflammatory cells and found to be present in atherosclerotic plaques. In this study, the predictive value of myeloperoxidase was assessed in 604 consecutive patients presenting to an emergency department with 24 hours or less of chest pain. All patients had a single baseline myeloperoxidase level drawn, then were followed up for 6 months for the combined endpoint of myocardial infarction (MI), coronary revascularization, or death.

Findings

Patients were stratified into quartiles by their baseline level of myeloperoxidase, and it was found that the incidence of myocardial infarction increased with increasing quartiles of myeloperoxidase; 13.9% of patients in quartile 1 had MI, 16.6% of patients in quartile 2, 25.2% in quartile 3, and 38.4% in quartile 4 ($P < .001$ for trend). Baseline myeloperoxidase levels also predicted the risk of major adverse cardiac events over the following 30-day and 6-month periods. The investigators also found that plasma myeloperoxidase levels predicted cardiovascular risks independently of the levels of C-reactive protein and other markers of inflammation.

Patients were stratified into quartiles by their baseline level of myeloperoxidase, and it was found that the incidence of myocardial infarction increased with increasing quartiles of myeloperoxidase.

Prognostic Value of Placental Growth Factor in Patients with Acute Chest Pain

Heeschen C, Dimmeler S, Fichtlscherer S, et al.

JAMA. 2004;291:435-441.

In the second study, the protein placental growth factor (PlGF) was studied. PlGF is a member of the vascular endothelial growth factor family, which is believed to act as a primary inflammatory mediator of atherosclerotic plaque instability. The study objective was to determine whether blood levels of PlGF could predict risk for death or nonfatal myocardial infarction in patients with acute chest pain. The study population was a group of 547 patients with angiographically documented acute coronary syndrome enrolled in the CAPTURE (c7E3 Fab Anti-Platelet Therapy in Unstable Refractory Angina) trial in Europe, as well as a prospective cohort of 626 patients presenting to an emergency department with acute chest pain. All patients had a single baseline PlGF level and then were followed up for 30 days.

In patients with acute coronary syndrome, elevated PlGF levels indicated a significant increased risk of nonfatal myocardial infarction or death at 30 days.

Findings

In patients with acute coronary syndrome, elevated PlGF levels indicated a significant increased risk of nonfatal myocardial infarction or death at 30 days (14.8% vs 4.9% $P < .001$). In multivariate analysis, elevated levels of PlGF, a marker of inflammation, was an independent predictor of risk (hazard ratio [HR], 3.03; $P < .001$). Elevated levels of troponin T, a marker of myocardial necrosis, was also an independent predictor of risk (HR, 1.83; $P = .03$); and elevated levels of soluble CD40 ligand, a measure of platelet activation, was an independent predictor of risk (HR, 2.65; $P = .002$), and conversely, high-sensitivity C-reactive protein level was not.

Commentary

These two studies both address novel markers for risk prediction in the setting of chest pain of unknown origin or chest pain with documented acute coronary syndromes. The first study finds myeloperoxidase to be an independent predictor of short-term risk of myocardial infarction and longer-term risk of adverse cardiac events. The second study finds that the inflammatory marker PlGF is an independent predictor of risk of nonfatal myocardial infarction or death in the setting of an acute coronary syndrome. Although these and other data are compelling in identifying novel risk markers,[2] the optimal tests to identify high-risk patients with chest pain have yet to be determined. It appears likely that in the near future, we will determine a battery of tests that best identifies risk. This would allow more efficient triaging of chest pain patients in the emergency room and more effective treatment of high-risk patients with acute coronary syndromes. ■

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