Low Copeptin Level Effectively Ruled Out MI

Copeptin levels were highest among patients who were later confirmed to have ST-elevation MIs.

BY MITCHEL L. ZOLER

ORLANDO — Adding a new serum stress-marker test to the standard cardiac troponin assay allowed researchers to rule out acute myocardial infarction with nearly 100% accuracy in 756 chest-pain patients who presented to the emergency department.

An acute MI screening protocol that includes the new test for the stress marker copeptin plus the test for cardiac troponin, as well as ECG results and clinical findings, "may obviate the need for prolonged stay in the emergency department and troponin retesting after 6 hours in [about] two-thirds of patients," a step that could have significant medical and economic benefits, Dr. Tobias Reichlin said at the annual meeting of the American College of Cardiology.

"A holy grail has been a simple blood test that works early on" to rule out acute MI, noted Dr. Christopher P. Cannon, a cardiologist at Brigham and Women's Hospital, Boston.

The test for copeptin looks "very promising" as part of an early screen, he added.

Copeptin is the C-terminal peptide that's removed from the vasopressin prohormone, and is a surrogate marker for endothelial stress, said Dr. Reichlin, a researcher in the biomedicine department at the University of Basel (Switzerland). Copeptin is stable ex vivo for several days, and in healthy people exists in the blood at a median concentration of about 4 pmol/L.

The Advantageous Predictors of Acute Coronary Syndromes Evaluation study examined the efficacy of using copeptin with serum levels of cardiac troponin to rule out MI in chest pain patients seen in the emergency departments of several centers during April 2006–April 2008. A final adjudicated diagnosis that was made independently by two cardiologists identified 131 patients (17%) as definitely having an acute MI. About two-thirds of those patients had a non–ST-elevation MI; the rest had an ST-elevation MI. The remaining 625 patients who were seen in the emergency departments included 46% with noncardiac chest pain, 16% with unstable angina, 13% with noncoronary cardiac chest pain, and 9% with chest pain of unknown origin. (Percentages add up to 101% because of rounding.) Their average age was 62 years, and about two-thirds were men.

Copeptin levels were significantly highest among patients who were later confirmed to have ST-elevation MIs, and were significantly elevated in patients with non–ST-elevation MIs, compared with those who had other types of chest pain.

Adding the test for copeptin 'could have significant medical and economic benefits.'

DR. REICHLIN

During the first 4 hours after symptom onset, the copeptin level averaged 32 pmol/L among the MI patients. During the same period, cardiac troponin levels remained low, averaging 4 mcg/L. More than 10 hours after symptom onset, the average copeptin level in the MI patients fell to about 10 pmol/L, whereas the average troponin level rose to about 30 mcg/L.

An analysis of the diagnostic accuracy of copeptin and troponin levels together by a receiver-operator curve showed that measuring those two analytes could account for 96% of the MI diagnoses.

A copeptin-level cut point of 14 pmol/L, combined with a standard troponin cut point, produced a sensitivity for diagnosing MI of 97.7% and a specificity of 76.3%, resulting in a negative predictive value of 99.4% and a positive predictive value of 46.4% in the 756 patients studied, Dr. Reichlin said. If the analyte criteria had been applied to those patients, two-thirds could have been discharged from the emergency department with an MI ruled out.

Although the results look promising for copeptin, Dr. Reichlin acknowledged that the study cohort was too small to allow a definitive conclusion about the ability of copeptin plus cardiac troponin to rule out patients without an MI, he said.

The study, investigator initiated, received no commercial funds. Dr. Reichlin reported no conflicts of interest. ■

Mortality Slashed, Diagnoses Steady, Long-Term Data Show

BY ELIZABETH MECHCATIE

Two retrospective reviews reveal trends in acute myocardial infarction and mortality associated with cardiogenic shock in hospitalized patients.

One study compared incidence and survival rates of initial acute myocardial infarction (AMI) diagnosed either by ECG or by serum biomarkers, in 9,824 men and women aged 40-89 years, in the Framingham Heart Study between 1960 and 1999. Of the 941 first AMIs documented during this time, 639 (68%) were diagnosed with an ECG and 302 (32%) were diagnosed with a biomarker.

During this time, there was a 50% drop in the rates of AMI diagnosed with ECGs. But the rates of AMI diagnosed with biomarker measurements increased by about twofold, "offering a possible explanation for apparently steady national rates of overall AMI in the face of improvements in primary prevention," the authors concluded (Circulation 2009;119:1203-10).

'The advent of increasingly sensitive biomarkers for AMI has substantially influenced AMI detection rates in the United States over the past several decades.'

Significant reductions in AMIs diagnosed by ECGs were noted among men aged 50-59 years, men aged 70-79 years, and women aged 70-79 years. Statistically significant increases in AMIs diagnosed with biomarkers were seen among men aged 50-59 and 70-79, and among women aged 70-79. Changes among AMIs in both categories were "largely flat" for those aged 60-69, they said.

"The advent of increasingly sensitive biomarkers for AMI has substantially influenced AMI detection rates in the United States over the past several decades," concluded the authors, led by Dr. Nisha I. Parikh of the National Heart, Lung, and Blood Institute's Framingham (Mass.) Heart Study, and Beth Israel Deaconess Medical Center, Boston.

"National MI trend data may be biased by a diagnostic drift resulting from the advent of diagnostic biomarker tests for AMI," they said, adding that this "may explain the paradoxical stability of AMI rates in the United States despite concomitant improvements in CHD risk factors."

In addition, 30-day, 1-year, and 5-year AMI case fatality rates dropped by 60% between 1960 and 1990, a highly statistically significant effect, with parallel declines observed for both AMIs diagnosed with ECG and those diagnosed with biomarkers.

"The marked improvements in the short- and long-term prognosis associated with AMI likely reflect advances in medical care and greater use of evidence-based cardiac therapies," Robert J. Goldberg, Ph.D., professor of medicine and epidemiology at the University of Massachusetts, Worcester, wrote in an editorial (Circulation 2009;119:1189-91).

Dr. Goldberg was the lead author of the second study, which analyzed trends in hospital mortality from cardiogenic shock complicating AMI—the most common cause of death in hospitals associated with AMI—among patients enrolled in the Worcester (Mass.) Heart Attack study.

Of the more than 13,000 people hospitalized with an AMI in the Worcester metropolitan area during 15 annual periods between 1975 and 2005, 6.6% developed cardiogenic shock.

The incidence of cardiogenic shock associated with AMI was relatively stable between 1975 and the late 1980s, at an average 7.5%.

Subsequently, the incidence was "somewhat inconsistent," until 1990, when the rate dropped to 4.8%, and reached a low of 4.1% in 2003.

This lower incidence of cardiogenic shock is "all the more impressive" considering that the patient population has gotten much older and diabetes, heart failure, and other serious comorbidities have become more common, noted Dr. Goldberg and his associates (Circulation 2009;119:1211-9).

About 65% of those who developed cardiogenic shock died in the hospital, compared with 11% of those who did not develop cardiogenic shock, a significant increased risk of death during hospitalization. Over the 30-year period, the risk of dying in the hospital was nearly 18 times greater among those who developed cardiogenic shock than among those who did not. In patients hospitalized during 2003 and 2005, the mortality risk among those with cardiogenic shock remained high, although the absolute risk was lower: 12.5 times greater than those who did not develop cardiogenic shock.

Short-term death rates dropped significantly during the period studied: In 1975 and 1978, 76% of patients who developed cardiogenic shock and 16.5% of those who did not died in the hospital. But in 2003 and 2005, 45% of those who developed cardiogenic shock died while in the hospital, compared with 7% of those who did not. In 2003 and 2005, hospital mortality associated with cardiogenic shock increased with older age, from nearly 36% in patients aged 65-74 years, to 57% in those aged 75-84 and almost 65% in those aged 85 years and older.

Noting that the rate of cardiogenic shock after AMI remains relatively high, despite apparent drops over the past 30 years, the authors wrote, "it remains to be seen whether current efforts aimed at reducing the extent of prehospital delay and door-to-balloon times may lead to further declines in the incidence" and fatality rates.

None of the other authors of the two studies had conflicts of interest to report.

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