Biomarker trio predicts near-term heart risk

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The annual risk of heart attack or death is more than five times greater for individuals in the highest risk group compared to those in the lowest risk group, according to data from more than 3,400 patients over an average follow-up time of 2.3 years.

(Medical Xpress)—Cardiologists have identified a trio of biomarkers that may predict which patients with heart disease have a high risk of heart attack or death in the next two years.

"The information supplied by this test could give physicians more clarity in deciding which patients with a history of heart disease need extensive diagnostic testing and more aggressive medical therapy," says Arshed Quyyumi, MD, professor of medicine (cardiology) at Emory University School of Medicine and co-director of the Emory Clinical Cardiovascular Research Institute. "It will also help identify low-risk patients who can now avoid unnecessary tests and treatments."

Together, measurements of the biomarkers form a risk score, from zero

to three. The annual risk of heart attack or death is more than five times greater for individuals in the highest risk group compared to those in the lowest risk group, according to data from more than 3,400 patients over an average follow-up time of 2.3 years.

The research was a collaboration among investigators at Emory, MedStar Health and FirstMark, a division of the San Diego firm Genway Biotech. The results were published this week in the *Journal of the American College of Cardiology*.

Quyyumi and Stephen Epstein, MD are co-senior authors. Epstein is director of Translational and Vascular Biology Research at MedStar Heart Institute and clinical professor of medicine at Georgetown University. Danny Eapen, MD, a cardiology research fellow at Emory, is first author of the paper.

FirstMark is developing the trio of biomarkers as a commercial test, called "PREvent."

The new risk score contrasts with the Framingham Risk Score, which calculates someone's risk of developing heart disease over the next ten years. The trio of biomarkers provides the risk that someone who may already have coronary heart disease will have a heart attack or die in the next few years.

"We expect this will be useful for all patients with known or suspected coronary artery disease, such as people in the group whom we studied, who were undergoing evaluation in the catheterization lab," Quyyumi says. "It could potentially be useful in all patients who would be considered high risk compared to the general population."

Researchers calculated the risk score for 3,415 patients at Emory who were undergoing cardiac catheterization for suspected coronary artery

disease from 2003 to 2009. Of this group, 12 percent were having a heart attack at the time of their examination. However, the outcomes were the same whether that sub-group was included or excluded.

The biomarkers were chosen in an effort to find indicators of "vulnerable plaque," atherosclerotic plaque that is likely to break off and form a blood clot.

"It has been difficult to differentiate between the person with heart disease who has stable plaque, and not at high risk, versus the patient with unstable plaque, which is vulnerable to rupture and at very high risk for a heart attack," Quyyumi says. "A large proportion of the group did not have a significant blockage as seen by angiography, yet some of those people may have had vulnerable plaque."

[Emory researchers are also looking at how the anatomy and curvature of the coronary arteries, which cannot be assessed by measuring levels of a blood protein, contribute to determining where vulnerable plaque will form via fluid dynamics.]

The three biomarkers are:

- CRP (C-reactive protein), an indicator of inflammation
- HSP70 (heat shock protein 70), an indicator of cellular stress
- FDP (fibrin degradation products), an indicator of blood clotting activity

The level of each protein in the blood is measured and if each one is higher than a certain threshold, that will contribute one to the risk score. In the Emory group, a patient who tested positive for all three had a 16.3 percent probability of experiencing a heart attack or dying within one year, compared to a 2.4 percent rate for those with no positive

biomarkers.

By itself, CRP has been proposed as a potential guide for doctors in deciding whether to treat patients with cholesterol-lowering statins. CRP does predict heart disease-related events with a moderate strength, Quyyumi says. However, high CRP levels can also be a sign of cancer, lung disease, or some other form of inflammation not related to heart disease. Adding the other two markers helps provide more specificity, he says.

   More information: Eapen, D. et al. Aggregate Risk Score Based on Markers of Inflammation, Cell Stress, and Coagulation is an Independent Predictor of Adverse Cardiovascular Outcomes. *J. Am. Coll. Cardio*, in press (2013). www.sciencedirect.com/science/ … ii/S0735109713017968

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