Biomarkers' ability to improve prediction of cardiovascular risk is modest

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Measurement of known biomarkers of cardiovascular disease slightly improves the ability to predict future heart attack or stroke in healthy individuals, but not enough to change preventive therapies. The study led by investigators at Massachusetts General Hospital (MGH) and Lund University in Sweden appears in the July 1 *Journal of the American Medical Association*.

"While there currently does not appear to be a role for routine use of biomarkers in screening for cardiovascular risk, our data do not exclude a role for biomarkers in selected patients," says Thomas Wang, MD, of the MGH Heart Center, the study's senior and co-corresponding author. "We're still optimistic that new technologies will lead to the discovery of biomarkers that could help us move toward offering truly personalized cardiovascular risk prediction."

Although conventional risk factors - such as smoking, hypertension, cholesterol levels and age - can identify individuals at the highest risk for heart attack or stroke, many people without these factors still experience these potentially devastating events. Since preventive measures such as lifestyle modification and the use of statin drugs to control elevated cholesterol can reduce risk, the authors note, it is essential to identify people whose risk could be reduced by behavioral or therapeutic steps. Some previous studies of the prediction of cardiovascular risk by biomarkers - laboratory measurements reflecting biological states that could have prognostic utility - focused on groups already known to be at high risk and others did not examine whether information provided by

biomarkers could actually change an individual's risk classification. The current study was designed to address those limitations.

The investigators focused on two biomarkers that have been extensively studied in cardiovascular disease - C-reactive protein (CRP) and N-terminal pro-B-type natriuretic peptide (N-BNP) - and four that recently have been identified as relating to cardiovascular risk - Cystatin C, Lp-PLA2, MR-proADM and MR-proANP. They enrolled more than 5,000 participants in the Malmö Diet and Cancer Study (MDC), an ongoing prospective study based at Lund University, for whom both complete conventional cardiovascular risk data and plasma samples were available. The investigators analyzed plasma levels of the six biomarkers in samples taken when participants entered the MDC and then, using a personal identification number assigned to each Swedish citizen, searched for information on subsequent coronary and cardiovascular events in databases on hospital discharges, strokes and causes of death occurring over a period averaging almost 13 years.

Two of the studied biomarkers - N-BNP and MR-proADM - did significantly improve the prediction of coronary events, defined as a heart attack or death from ischemic heart disease. N-BNP and C-reactive protein improved the prediction of cardiovascular events, which are coronary events plus strokes. But when the ability of biomarkers to move individual patients into higher- or lower-risk categories was analyzed, the potential impact on treatment decisions was minimal.

"Since choice of therapies may depend on the risk category a patient falls into, moving patients between risk categories could lead to a change in therapy," explains co-author Christopher Newton-Cheh, MD, MPH, MGH Heart Center. "While there was more category movement among participants initially classified as intermediate-risk, that resulted primarily from movement to lower risk levels, so we still need to find biomarkers that can make a clinically significant difference in predicting

cardiovascular risk." Wang and Newton-Cheh are both assistant professors of Medicine at Harvard Medical School.

Source: Massachusetts General Hospital