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News & Information for Medical Professionals

High- Sensitivity CRP Enhances Risk Prediction for Heart Disease

High-sensitivity C-reactive protein modestly improves prediction of global cardiovascular risk beyond traditional risk factors, according to two longitudinal studies.

An algorithm incorporating the inflammatory marker and parental history improved risk prediction 5.3% overall and 14.2% for patients at intermediate risk by traditional risk scores (both $P<0.001$), found Paul M. Ridker, M.D., of Brigham and Women's Hospital, and colleagues.

Their analysis of the Physicians' Health Study II was reported at the American Heart Association meeting, last week. And in an analysis of the Framingham Heart Study, reclassifying risk based on hs-CRP improved prediction of cardiovascular disease by 5.6% ($P=0.014$) and of coronary heart disease by 11.8% ($P=0.009$), Peter W.F. Wilson, M.D., of Emory in Atlanta, and colleagues reported online in *Circulation: Cardiovascular Quality and Outcomes*.

These findings followed on the heels of the JUPITER trial, which showed that intensive lipid lowering with rosuvastatin (Crestor) in an "apparently healthy" population reduced the rate of MI, stroke, revascularization, and cardiovascular death 44% ($P<0.00001$) within two years.

In that trial, patients with LDL cholesterol levels below 130 mg/dL were treated on the basis of elevated hs-CRP levels, stirring debate over whether the marker should be used as a basis for making treatment decisions for low-risk patients.

Guidelines recommend hs-CRP only as an add-on test to refine risk prediction in patients with low to intermediate risk. Results from the three studies provide the strongest evidence to date that the hs-CRPn blood test is a useful marker for cardiovascular disease, according to a statement by Elizabeth G. Nable, M.D., director of the National Heart, Lung, and Blood Institute, which funded both longitudinal analyses.

"These findings suggest that adding high-sensitivity C-reactive protein levels to traditional risk factors could identify millions more adults for whom treatment with statins appears to lower the risk of heart attack," she said.

Dr. Nabel said the institute planned to analyze the findings and has already engaged an expert panel to generate comprehensive, evidence-based clinical guidelines for primary-care practitioners.

Dr. Wilson's group recommended a two-step approach for clinical decisions that require risk assessment, using traditional risk scores first, then turning to hs-CRP levels as a tiebreaker for those at intermediate risk.

They analyzed baseline risk factors and used these to predict incident events over 12 years among the 3,006 participants in the offspring cohort of the Framingham Heart Study who were free of cardiovascular disease at baseline.

In the multivariate analysis, log hs-CRP was a significant predictor for MI and coronary heart disease-related death, considered "hard" coronary heart disease events (HR 1.34, 95% confidence interval 1.14 to 1.58) and total cardiovascular disease, which additionally included angina, transient ischemic attack, stroke, and intermittent claudication (HR 1.26, 95% CI 1.12 to 1.40).

When traditional risk factors -- age, sex, systolic blood pressure, total and HDL cholesterol, diabetes, current smoking, hypertension treatment, and homocysteine -- were included, log hs-CRP levels remained significant but provided little improvement in the discrimination of events.

This result suggested hs-CRP testing would not measurably improve initial screening for vascular disease risk, Dr. Wilson's group said. But it did modestly add to prediction by shifting patients into the correct risk category more often than not with a net reclassification improvement of 5.6% for total cardiovascular disease (P=0.014) and of 11.8% for hard coronary heart disease events (P=0.009).

The study also looked at homocysteine as a predictor, but in multivariate models these levels were associated only with hard coronary heart disease events with hazard ratios in the 0.53 to 0.62 range and not with total cardiovascular disease.

Dr. Ridker's study also looked at hs-CRP as a predictor but in conjunction with genetic risk indicated by parental history of MI along with other traditional risk factors in the Reynolds risk score.

Their analysis of the Physicians' Health Study II included 10,724 male health professionals without baseline heart disease or diabetes who were followed prospectively over a mean 10.8 years.

Compared with the traditional model based on age, blood pressure, smoking status, and total and HDL cholesterol, the model that included hs-CRP and parental history significantly improved prediction (P<0.001).

For prediction of all types of cardiovascular events, the Reynolds risk score reclassified risk for 17.8% of participants overall and 20.2% of those at intermediate (5% to 20%) 10-year risk, with "markedly improved accuracy among those reclassified."

The improvement in net reclassification index was 5.3% and 14.2% for the clinically relevant group of patients at intermediate risk (both P<0.001).

For coronary heart disease prediction in men not on a statin, the algorithm improved the accuracy of the risk category for the 16.7% of participants reclassified and the 20.1% of those at intermediate 10-year risk (P<0.001).

The net reclassification index in this group was 8.4% overall and 15.8% for those previously classified as at intermediate risk (both P<0.001).

Practice Pearls:
Explain to interested patients that the studies supported incorporation of hs-CRP into clinical cardiovascular risk prediction algorithms
Note that the NHLBI is reviewing evidence from the studies for incorporation into clinical guidelines

Ridker PM, et al "C-Reactive Protein and Parental History Improve Global Cardiovascular Risk Prediction: The Reynolds Risk Score for Men" Circulation 2008; 118: DOI: 10.1161/CIRCULATIONAHA.108.814251.

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FACT:

Higher Nonfasting Triglycerides Linked With Increased Stroke Risk:A new study finds an association between higher levels of nonfasting triglycerides and increasing risk for ischemic stroke. Using a nonfasting measure of triglycerides in a large population, the researchers report a "previously unnoticed" association between linear increases in triglycerides and a stepwise increase in the risk for ischemic stroke. See This Weeks Item #11
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