Framingham Score Not Aided by CRP Results

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CHICAGO – Measurement of high-sensitivity C-reactive protein had little to no utility in refining cardiovascular risk assessment beyond that provided by the classic risk factors in a new secondary analysis of ASCOT, throwing into question the biomarker's appropriate role in clinical practice.

"In the ASCOT–Lipid Lowering Arm, neither baseline nor on-treatment CRP provided any useful information about the efficacy of statin treatment to reduce cardiovascular events beyond LDL cholesterol reduction. These results do not support current proposals to measure CRP in the clinical setting, either to assign statins to individuals on the basis of an elevated CRP alone or to monitor

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DR. SEVER

CRP levels as an indicator of the efficacy of statin treatment," Dr. Peter S. Sever said at the meeting.

In ASCOT (the Anglo-Scandinavian Cardiac Outcomes Trial), combining a baseline determination of CRP with a standard Framingham Risk Score did not significantly enhance the ability to predict future cardiovascular disease events beyond that provided by Framingham score alone. And, while once patients were on statin therapy, the resultant reduction in LDL was associated with an impressive 55% reduction in cardiovascular events compared with placebo, the decrease in CRP was not linked to a significant decrease in such events, according to Dr. Sever, professor of clinical pharmacology and therapeutics at Imperial College, London.

ASCOT was a landmark primary prevention trial in which nearly 20,000 hypertensive patients were randomized to one of two antihypertensive regimens, then the 10,305 participants with a total cholesterol level of 250 mg/dL or less were re-randomized to 10 mg/day of atorvastatin (Lipitor) or placebo. Although this was a primary prevention trial, these were high-risk patients with three other cardiovascular risk factors in addition to hypertension and a mean 28% risk of developing cardiovascular disease within the next 10 years based upon their Framingham Risk Score.

The new retrospective ASCOT analysis involved 485 patients who experienced a coronary event or stroke during 3.3 years of follow-up and 1,367 controls who did not. Analyzing the data with use of four different statistical methods, neither baseline CRP nor change in CRP level after 6 months of statin therapy provided any practical information.

"I think our conclusion is fairly clear: In patients with hypertension, they're on statins. In patients with diabetes, they're on statins. In patients with stable coronary artery disease, they're on statins. There's no added benefit to be gained from measuring CRP," Dr. Sever said.

Discussant Dr. Donald Lloyd-Jones said that "the ASCOT data are the latest adding to a large body of literature suggesting minimal clinical utility for CRP in risk assessment and decision making for lipid-lowering therapy, and a small, growing, and frankly mixed literature examining the utility of on-treatment CRP levels," observed Dr. Lloyd-Jones, professor of preventive medicine at Northwestern University, Chicago.

In ASCOT, patients with an on-treatment LDL below the median had a reduced cardiovascular event risk regardless of their CRP level, while those with a higher LDL had a higher risk regardless of their CRP level. And among patients with a low on-treatment LDL, having a low CRP was not associated with additional benefit, he noted.

Factoring in baseline CRP resulted in a net reclassification improvement score, or NRI, of 0.005 in ASCOT participants at intermediate risk on the basis of their

Framingham score. The NRI is a recently developed measure that has been embraced by preventive medicine because it expresses how useful a novel cardiovascular risk factor is in further defining Framingham intermediate-risk patients as either high- or low-risk. The NRI for baseline CRP in ASCOT was weak and nonsignificant. By contrast, the NRI for coronary artery calcium score in Framingham intermediate-risk patients in the Multi-Ethnic Study of Atherosclerosis (MESA) was a robust 0.55, more than two orders of magnitude greater than for CRP in ASCOT.

ASCOT is just the latest in a growing number of studies that raise a central question, he added: "Is CRP something we need to be spending our time on?"

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DR. LLOYD-JONES

So how often does Dr. Lloyd-Jones obtain a CRP in his own clinical practice? "Never," he said in an interview.

Asked to comment, Dr. Christopher Cannon of Brigham and Women's Hospital, Boston, said his interpretation of the ASCOT results is that in patients who already have a good indication for statin therapy, knowing the baseline CRP level does not provide additional useful information.

"Once you get into places where you should be treating anyway, then CRP is not helpful. But in the JUPITER trial they had patients largely without other risk factors, and in that lower-risk group a high baseline CRP picked out those who would benefit from statin therapy," Dr. Cannon explained.

He agreed with Dr. Sever and Dr. Lloyd-Jones that the message from ASCOT regarding the use of on-treatment CRP to titrate statin therapy is that it doesn't make sense.

Dr. Sever declared that he is a consultant to and is on the speakers bureau for Pfizer, which sponsored ASCOT. Dr. Cannon is also on the speakers bureau for Pfizer. Dr. Lloyd-Jones reported no relevant financial interests. ■