To Reduce CRP, Look Beyond LDL Lowering

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ORLANDO, FLA. — Switching from a standard-dose statin to intensive statin therapy often lowers C-reactive protein by one-third to one-half in patients with acute coronary syndrome. But what if that's not enough?

What is a physician to do when a high-risk patient's C-reactive protein (CRP) level—an important marker of cardiovascular risk—remains elevated despite maximal-dose statin therapy?

That's the most common question that Christopher P. Cannon, M.D., has fielded from physicians since he presented the findings of the landmark Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 (PROVE IT–TIMI 22) trial last year.

And the answer, based on a new secondary analysis of PROVE IT, is straightforward: Redouble efforts to achieve control of the standard cardiovascular risk factors.

The PROVE IT data show that even in the current era of intensive statin therapy for the highest-risk patients, the conventional cardiovascular risk factors remain extremely important, he said at the annual meeting of the American College of Cardiology.

"The more risk factors you have, the higher your CRP. And the converse is true, too. The fewer risk factors you have which are out of control, the lower your CRP," reported Dr. Cannon of Brigham and Women's Hospital and Harvard Medical School, Boston.

The new PROVE IT analysis showed that being a current smoker was independently associated with a 50% increase in CRP level, compared with that of nonsmokers.

Similarly, each of six additional modifiable cardiovascular risk factors was associated with increases in CRP between 10% and 40%.

The six modifiable cardiovascular risk factors were a body mass index greater than 25 kg/m^2, an HDL-cholesterol level of less than 50 mg/dL, an LDL-cholesterol level of 70 mg/dL or greater, a blood glucose level greater than 110 mg/dL, blood pressure in excess of 130/85 mm Hg, and a triglyceride level above 150 mg/dL.

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These are observational data. Patients who participated in the PROVE IT trial weren't randomized to smoking cessation, weight loss, or other lifestyle interventions.

But the suggestion from these data is that control of the conventional modifiable risk factors is the logical next step in reducing CRP once a high-risk patient is on 80 mg/day of atorvastatin or its equivalent, Dr. Cannon said.

"The metabolic risk factors are major drivers of inflammation. And these data say that even in the presence of the most intensive statin therapy we can provide, doing multiple risk factor modification looks like it will further improve things," Dr. Cannon observed.

In a similar way, even in patients who are doing everything correctly in terms of controlling their modifiable cardiovascular risk factors, cranking up the dose of their statin will further substantially reduce their CRP concentration, he added.

Dr. Cannon said that he has come to view CRP as "a global barometer" of cardiovascular risk factor burden.

"It's one number that accounts for everything and can be a simple way to track how you're doing," Dr. Cannon explained.

Based on these new PROVE IT findings regarding the likely importance of controlling standard cardiovascular risk factors as an additional means of lowering CRP in patients on intensive statin therapy, investigators are interested in planning and executing a definitive, randomized controlled trial looking at aggressive multi–risk-factor reduction in combination with maximal-dose statins, Dr. Cannon added. ■