If CRP Remains High, Target CVD Risk Factors

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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) concentration—an important marker of cardiovascular disease risk—remains elevated, despite use of 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, Dr. Cannon 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 a 10%-40% increase in CRP concentration.

These risk factors were a body mass index greater than 25 kg/m^2, an HDL-cholesterol concentration of less than 50 mg/dL, an LDL-cholesterol level of 70 mg/dL or greater, a blood glucose concentration 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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DR. CANNON

These are observational data; participants in PROVE IT 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 cardiovascular risk factors is the logical next step in reducing CRP concentration once a high-risk patient is taking 80 mg/day of atorvastatin or its equivalent.

"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.

Similarly, even in patients who are doing everything right 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 he has come to view CRP as "a global barometer" of the cardiovascular risk factor burden.

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

These new PROVE IT findings demonstrate the likely importance of controlling standard cardiovascular risk factors as an additional means of lowering CRP concentration in patients on intensive statin therapy.

On the basis of the PROVE IT results, there is investigator interest in conducting a definitive, randomized controlled trial that will look at aggressive multi-risk-factor reduction in combination with maximal-dose statins, Dr. Cannon added. ■