

# Addition of C-Reactive Protein Levels to Framingham Proposed

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NEW YORK — The predictive value of the Framingham risk score could change substantially if serum C-reactive protein levels were included in the calculation.

An analysis of data collected on more than 15,000 women in the Women's Health Study showed that incorporating C-reactive protein (CRP) levels into the Framingham risk score significantly alters the risk estimate for nearly a third of women whose 10-year risk of a coronary event was 5%-9.9% without CRP in the risk equation. Among women whose baseline risk without CRP predicted a 10%-19.9% risk of a coronary event, adding CRP information significantly changed the risk for 42% of these women, Paul M. Ridker, M.D., said at an international symposium on triglycerides and HDL.

The redefined risk level can move either up or down, said Dr. Ridker, director of the Center for Cardiovascular Disease Prevention at Brigham and Women's Hospital in Boston.

This impact of CRP could potentially have an immediate effect on patient management and provides a rationale for immediately adding CRP to the traditional risk factors that make up the Framingham risk score.

"The issue is lifestyle change," said Dr. Ridker at the symposium, sponsored by the Giovanni Lorenzini Medical Foundation. CRP levels may be able to get primary care physicians to say to patients that they need to lose weight, watch their diet, and exercise more because patients with a high serum level of CRP may have a higher risk than their LDL-cholesterol level indicates.

"These new data show that you can refine your estimates of who to treat and who not to treat," commented Steven E. Nissen, M.D., medical director of the Cardiovascular Coordinating Center at the Cleveland Clinic Foundation. Using CRP levels to help determine who needs treatment with, for example, a statin, may cut unneeded treatment from low-risk patients and may better target treatment to higher risk patients, he said.

The Framingham risk score is used to deter-

mine which patients, who do not have established coronary disease, should start statin and aspirin therapy. According to the Adult Treatment Panel III guidelines of the National Cholesterol Education Program, people with a 10-year risk of a coronary event of 10% or more, as calculated by the Framingham risk score, should start statin therapy if their serum level of LDL cholesterol is at least 130 mg/dL. If their risk score is less than 10%, then statin therapy is not recommended unless their serum LDL cholesterol is 160 mg/dL or higher. Guidelines from the U.S. Preventive Services Task Force say that people without proven coronary disease who have a 5-year risk of 3% or more should start daily treatment with aspirin.

The Women's Health Study enrolled 15,632 healthy women with an average age of 54 into a placebo-controlled trial that assessed the efficacy of treatment with aspirin and vitamin E. During an average follow-up of 10 years, 464 women developed a first-ever, confirmed cardiovascular end point. Among the parameters collected at baseline were serum CRP levels.

On the basis of these data, Dr. Ridker and his associates calculated that the 20% of women with the highest CRP levels at baseline (at least 4.2 mg/dL) had a nearly threefold increased risk of a cardiovascular event during the next 10 years, compared with the 20% of women with the lowest CRP levels (less than 0.5 mg/dL). This threefold increased risk of an event was calculated in a risk model that adjusted for all of the existing components of the Framingham risk score, showing that CRP was a significant predictor of risk, independent of the factors currently in the risk score, said Dr. Ridker, who is also a professor of medicine at Harvard University in Boston.

The analysis also showed that the ratio of total cholesterol to HDL cholesterol was at least as good for predicting risk of cardiovascular events as a ratio of apolipoprotein B-100 to HDL lipoprotein cholesterol (JAMA 2005;294:326-33).

Dr. Ridker is a coinventor on patents held by Brigham and Women's Hospital that relate to the use of inflammatory biomarkers in cardiovascular disease. ■

# Teen Hypertension Often Seen but Not Addressed

BY MARY ELLEN SCHNEIDER  
Senior Writer

SAN FRANCISCO — Physicians may be failing to address abnormal blood pressure levels among adolescents, according to a study presented at the annual meeting of the American Academy of Family Physicians.

The study analyzed blood pressure levels recorded on preparticipation sports physicals for more than 1,500 adolescents. More than 13% of the adolescents had either a hypertensive systolic or hypertensive diastolic blood pressure level, but few were identified as abnormal or provided with follow-up interventions, according to Kevin E. Burroughs, M.D., of the University of North Carolina, who conducted the study.

"If anything, we should be able to use this information to help us out with trying to help decrease morbidity and mortality for these individuals," Dr. Burroughs said.

His study looked at the preparticipation exams for 1,547 adolescents from three middle schools and three high schools in Cabarrus County, N.C., during the school years 2003-2004 and 2004-2005. He used guidelines from the National Heart Lung and Blood Institute's Working Task Force on Childhood Hypertension to classify the blood pressure by age and height.

As outlined in those guidelines, blood pressure values of greater than the 95th percentile for age, sex, and height were classified as

child and adolescent hypertension. Those in the 90-95th percentile were high normal blood pressure and blood pressure values that fell below the 90th percentile were considered normal.

Overall, 7.4% (114) of the adolescents in the study had systolic blood pressure that would be considered hypertensive and 6.5% (100) of the adolescents had a hypertensive diastolic blood pressure. But only 14 of the adolescents with hypertensive values were labeled as such, Dr. Burroughs said, and only 11 were scheduled for any follow-up.

Though hypertension is not determined by a single reading, it offers physicians an opportunity to identify at-risk individuals in a population that they don't frequently see in the office, Dr. Burroughs said.

"There's an alarmingly low number of abnormal values which have been labeled as such on this examination, possibly due to a lack of awareness among practitioners about these tables and considerations," he said.

Dr. Burroughs said he's spoken to a number of people who are unfamiliar with the guidelines for classifying blood pressure by age and height. Those familiar with the guidelines might find the process too time consuming, he said.

"We should be able to intervene for these people [by] including them in doing exercise programs, modifying their diet, before we have to get to the point of putting them on medication," he said. ■

**'We should be able to use this information to ... decrease morbidity and mortality for these individuals.'**

# Order of Meds Not Important

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treatment based on individual judgment of each patient," said Dr. Willenheimer, a cardiologist at University Hospital Malmö (Sweden). "For patients with tachycardia or ischemic cardiomyopathy, I'd start with a  $\beta$ -blocker," he told FAMILY PRACTICE NEWS.

Dr. Willenheimer has received honoraria from the German division of Merck, which sponsored the study and markets a formulation of the  $\beta$ -blocker bisoprolol (Concor) that is approved in many countries (but not the United States) for treating heart failure. In the United States, generic bisoprolol and its trade for-



mulation (Zebeta) are approved only for treating hypertension.  $\beta$ -Blockers approved for treating heart failure in the United States are carvedilol (Coreg) and metoprolol succinate (Toprol-XL).

**'A physician can start treatment based on individual judgment of each patient.'**

DR. WILLENHEIMER

ters in 20 countries. Their average left ventricular ejection fraction was 29%. Patients were randomized to start treatment with either 1.25 mg of bisoprolol once daily or 2.5 mg of the ACE inhibitor enalapril

b.i.d. Their monotherapy dosage was increased every 2 weeks until the bisoprolol dosage was 10 mg once daily or the enalapril dosage was 10 mg b.i.d. Monotherapy was continued to a total duration of 6 months, after which the second drug was begun with a similar uptitration scheme. Patients were followed for an average of 1.2 years.

By all efficacy measures used, the bisoprolol-first strategy was not inferior to the enalapril-first regimen.

The study's primary end point was the time to first all-cause death or all-cause hospitalization. During follow-up on an intention-to-treat basis, these events occurred in 35.2% of patients in the bisoprolol-first arm and in 36.8% of those in the enalapril-first arm. On a per-protocol basis, the event rates were 32.4% in the bisoprolol-first patients and 33.1% in the enalapril-first group.

The results were also published in Sept. 2005 in the online edition of Circulation

(<http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.105.582320v1>).

The incidence of treatment-related adverse events was also similar in both groups. However, in patients treated with bisoprolol first, the results showed a trend toward an improved survival benefit and a trend toward a higher frequency of worsening heart failure requiring hospitalization, especially early in the study.

These findings are probably class effects, Dr. Willenheimer said. In both treatment groups, the drug that was started first was given in higher dosages during the combined therapy phase.

The study was limited by several factors, Dr. Dickstein noted. It was done on an open-label basis, it did not include patients with class IV disease, and patients were maintained on monotherapy for the relatively long period of 6 months. Nonetheless, he said that on the basis of the results, he believes that the two strategies probably have comparable efficacy and safety. ■