CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Nontraditional Risk Factors in CHD Risk Assessment

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Coronary heart disease is the leading cause of death in the United States. Numerous strategies exist for detection and treatment of asymptomatic persons at risk for CHD. Guides such as the ATP III and Framingham risk calculators consider factors including age, gender, blood pressure, total cholesterol, HDL level, and diabetes in determining an individual's 10-year risk for a coronary event.

Unfortunately, with traditional metrics, 31% of men and 7% of women (21 million people) are classified as intermediate risk for CHD (10%-20% risk over 10 years). Aggressive risk factor modification is clearly indicated for high-risk individuals and is definitely not indicated for low-risk individuals, but the decision regarding therapy in intermediate-risk persons is difficult given less-certain benefits to weigh against possible harms.

The U.S. Preventive Services Task Force recently released guidelines evaluating the utility of nine nontraditional risk factors in CHD assessment.

► **High-sensitivity C-reactive protein**
Of the tests evaluated by the USPSTF, hs-CRP is the most clinically promising. An elevated hs-CRP (greater than 3.0 mg/L) conveys a relative risk of 1.58 for CHD events. In addition, hs-CRP can reclassify intermediate-CHD-risk individuals, with 11% of men elevated to high risk and 12% of men dropped to low risk. No such reclassification was possible for intermediate-risk women.

Statin studies in patients with normal LDL cholesterol and elevated hs-CRP show benefit, but it is unclear whether this the result of lowered hs-CRP or other statin effects. Therefore, hs-CRP remains a promising tool without a sufficient evidence base for USPSTF recommendation.

► **Ankle-brachial index**
ABI, the ratio of dorsalis pedis to right brachial artery systolic blood pressure, is a marker of peripheral vascular disease (PVD), itself a high-risk CHD equivalent. Though 10% of females at intermediate risk for CHD can be increased to high risk based on a low ABI (< 0.9), no clinical outcome differences were noted related to this reclassification, leading the USPSTF to reject the use of ABI in establishing CHD risk.

► **Leukocyte count**
The USPSTF found no relationship between elevated leukocyte count and CHD events. Furthermore, the clinical utility of any link would be limited by the lack of specific interventions to lower leukocyte level.

► **Fasting blood glucose**
In nondiabetic patients, impaired fasting glucose (100-125 mg/dL) is a weak predictor of CHD risk. Only 1 of 10 studies evaluated by the USPSTF found even a weak association between elevated fasting blood glucose and CHD risk in nondiabetics. Glucose testing in nondiabetics, therefore, is not indicated in evaluating CHD risk.

► **Periodontal disease**
Periodontal disease – including gingivitis, periodontitis, tooth loss, and bony loss – is a weak independent risk factor for CHD, likely due to chronic inflammation. The CHD relative risk of the various oral diseases ranges from 1.24 for periodontitis to 1.34 for significant tooth loss. However, largely because of the heterogeneity of periodontal disease processes, difficulty with classification schemes, and unclear evidence of treatment effect, the USPSTF does not recommend routine preventive or therapeutic dental care for reducing CHD events.

► **Carotid intima-media thickness**
Carotid IMT is an independent CHD risk factor and can modestly improve the predictive value of traditional risk assessments. However, severe methodologic limitations prevent the USPSTF from recommending carotid IMT for CHD risk assessment. Most carotid IMT studies are in the research setting, leaving the accuracy of clinical measurements unknown. Furthermore, no evidence exists for a treatment effect of lowering carotid IMT or using carotid IMT for risk restratification. Carotid IMT, therefore, has a limited role in CHD risk prediction.

► **Coronary artery calcification score**
CAC score has only poor to fair evidence as an independent marker for CHD risk, based on studies with poor methodologic quality. Furthermore, the clinical utility of CAC score is limited by unclear effects of treatment in lowering CHD risk, as well as the radiation exposure involved in measuring the score.

► **Homocysteine**
There is conflicting evidence linking homocysteine levels to increased CHD risk, with some studies reporting a relative risk of 1.21 for each 5 mol/L increase. No attempt was made to risk stratify patients based on homocysteine levels with or without Framingham risk data. Studies evaluating folate, the treatment for elevated homocysteine levels in patients with known CHD, did not show prevention benefit, and studies for primary prevention using folate have not been performed.

► **Lipoprotein(a)**
Evidence exists for lipoprotein(a) as an independent risk factor for CHD, but no stratification of intermediate-risk patients was performed. Furthermore, the treatment effect of lowering elevated lipoprotein(a) is unclear independent of lowering LDL.

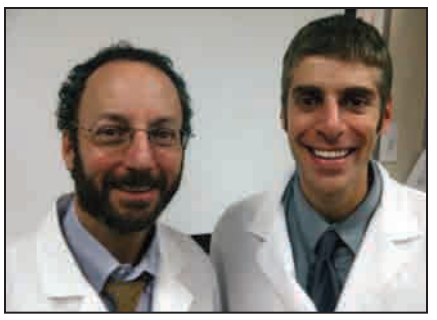
The Bottom Line

None of the nine risk factors studied meets the two main criteria for clinical utility: the restratification of a substantial number of intermediate-risk Framingham patients to high risk, and the changing of management of these patients in a manner that reduces CHD risk.

Some of the studied risk factors, including hs-CRP, homocysteine level, and CAC score, may be utilized in individual situations to better evaluate intermediate-risk Framingham patients.

Reference

Emerging Risk Factors for Coronary Heart Disease: A Summary of Systematic Reviews Conducted for the U.S. Preventive Services Task Force (Ann. Intern. Med. 2009;151:496-507).



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Rheumatoid Arthritis Boosts Stroke, Atrial Fibrillation Risk

BY MITCHEL L. ZOLER

FROM THE ANNUAL CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY

STOCKHOLM – Patients with rheumatoid arthritis had a significantly increased risk for developing stroke and atrial fibrillation compared with the general population, in a study of more than 11,000 rheumatoid arthritis patients.

The increased stroke risk in rheumatoid arthritis (RA) patients appeared independent of their increased likelihood for having atrial fibrillation, a known stroke risk factor, reported Dr. Jesper Lindhardsen.

The results "add to the growing awareness that RA patients need to be evaluated with respect to cardiovascular comorbidity," said Dr. Lindhardsen, an internist in the department of cardiology at Gentofte Hospital in Hellerup, Denmark. The recommended annual assessment of RA patients for cardiovascular disease and risk should include an ECG evaluation for atrial fibrillation and should also pay attention to stroke risk factors, he said in an interview.

His study used data that was collected in Danish national registries for about 4.2 million citizens who were older than age 16 years in 1997, excluding those with a prior diagnosis of RA, stroke, or atrial fibrillation. During the following 10 years, 11,038 people received a diagnosis of new onset RA.

The average age of the study population was 47 years in 1997, compared with an average age of 56 at the time of new RA diagnosis. The entire Danish population included 51% women, compared with 70% of those diagnosed with RA. Average follow-up for the entire group was 9 years; the average follow-up after RA diagnosis was 4 years. Among those with incident RA, 14% regularly took one or more cardioprotective drugs, roughly similar to the 10% rate in the entire population.

During follow-up, stroke occurred 41% more often in RA patients than in the general population, and atrial fibrillation occurred 45% more often. Both differences were statistically significant.

Age also had a significant impact on stroke risk but not on atrial fibrillation risk in the RA patients. The increased risk for atrial fibrillation in RA patients remained similar in people younger than 50 years, those aged 50-65 years, and in those older than 65 years.

In contrast, stroke risk ran more than 3-fold higher in RA patients younger than age 50 years compared with the general population. The stroke risk of RA patients who were aged 50-65 years ran 50% higher than in the general population, and RA patients older than 65 years had a 20% higher risk than did the general population.

Dr. Lindhardsen and his associates also used a case-control analysis of subjects with incident stroke to examine whether atrial fibrillation boosted the stroke risk of RA patients. They found similar risks in patients with RA alone and in those with RA and atrial fibrillation. ■

VITALS

Major Finding: Following diagnosis of rheumatoid arthritis, patients had a 45% increased risk for developing atrial fibrillation and a 41% increased risk for stroke compared with the general adult population without rheumatoid arthritis.

Data Source: Ten-year follow-up of national medical records for 4.2 million Danish citizens, including 11,038 with new-onset rheumatoid arthritis.

Disclosures: Dr. Lindhardsen said that he had no disclosures.