POEMs

Patient-Oriented Evidence that Matters

There appears to be some confusion about the use of biomarkers, in particular CRP and homocysteine, in the prediction of cardiovascular risk and in the management of patients with abnormal results. This reasonably large, population-based study helps to resolve some of these issues. Editor

Clinical question

Do new biomarkers improve our ability to predict whether a patient will have an initial cardiovascular event?

Bottom line

Novel biomarkers predict cardiovascular risk, but do not add to our current ability to predict risk using conventional risk factors like age, sex, cholesterol level, diabetes, tobacco use, and blood pressure. The new biomarkers should not be routinely used, given their cost and the fact that we do not know whether modifying these risk factors improves patient outcomes. (LOE = 1b)

Reference

Wang TJ, Gona P, Larson MG, et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. N Engl J Med 2006; 355:2631–2639.

Study Design

Cohort (prospective)

Funding

Government

Setting

Population-based

Synopsis

There is increasing attention in the popular media and among some physicians and their patients to new biomarkers for the prediction of cardiovascular risk. However, it is important to ask two questions: *Does a biomarker significantly improve our ability to predict risk over existing risk factors*; and, *Does this knowledge help us choose interventions that can modify risk?* The authors of this study identified 3209 men and women with a mean age of 59 years who were participating in the Framingham Offspring Study. Fasting levels of 10 biomarkers (C-reactive protein, B-type natriuretic peptide, N-terminal pro-atrial natriuretic peptide, aldosterone, renin, fibrinogen, D-dimer, plasminogen-activator inhibitor type 1, homocysteine, and the urinary albumin-to-creatinine ratio) were measured and patients were followed up for a median of 7.4 years. During that time, 207 patients died and 169 had a first major cardiovascular event (myocardial infarction, prolonged angina with electrocardiographic changes, heart failure, or stroke). A pair of multivariate models were developed to predict the risk of death and initial cardiovascular event. The model developed to predict risk of death included C-reactive protein, B-type natriuretic peptide, urinary albumin-to-creatinine ratio, homocysteine, and plasma renin; the model for initial cardiovascular event included only B-type natriuretic peptide and urinary albumin-to-creatinine ratio. The 'multimarker scores' generated by these models were stratified into three groups: low risk (bottom 40%), intermediate risk (middle 40%), and high risk (top 20%). The models were then adjusted for conventional risk factors like age, sex, cigarette use, cholesterol level, and diabetes. The multimarker scores accurately predicted cardiovascular risk, with a relative risk of death that was four times greater in the group with high scores than in the group with low scores. The researchers then compared risk prediction using only conventional risk factors with risk prediction using conventional risk factors plus the multimarker scores. Using the C-statistic and the area under the receiver operating characteristic curve, two overall measures of predictive accuracy, the authors found no significant difference between these sets of models (e.g. C-statistic = 0.76 for conventional risk factors vs C-statistic = 0.77 when you add the multimarker score to predict cardiovascular events).

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** Patient-Oriented Evidence that Matters. See editorial (NZFP 2003; 30:150)*