C-Reactive Protein and Electron Beam Tomography

To the Editor:

The study by Park et al1 demonstrates that electron beam tomography (EBT)–derived coronary calcium scores (CCS) are incremental in predicting cardiac risk, consistent with previous data. However, the authors downplay the prognostic power of CCS and elevate the value of C-reactive protein (CRP). They state, “CRP was a marginally significant predictor of MI [myocardial infarction] or coronary death (P=0.09),” and, “CRP continued to contribute to the prediction of cardiovascular events (P=0.07) for MI coronary death.” Are the authors suggesting that their predetermined level of significance of 0.05 is not correct? Lowering the standard for statistical significance will only increase the odds of a random event being deemed “significant.”

In this study, the predictive power of CCS constituted most of the risk prediction, as the relative risk of hard cardiac events increased from 1 to 4.9 with increasing calcium tertiles (P=0.005). Increasing CRP among patients with low CCS raised the relative risk from 1.0 to 1.7 (P=NS), and in the highest CCS tertile, from 4.9 to 6.1 (P=NS). CRP, in this study, was not a significant predictor of hard cardiac events.

The new National Cholesterol Education Program guidelines2 suggest that both of these new tests play a role in risk stratification. The most significant finding in the study by Park et al1 is that EBT-derived CCS is a potent predictor of cardiac events (P=0.0005), whereas CRP was only a modest predictor of total events (P=0.03). Additionally, the study by Park et al1 conspicuously avoids acknowledging EBT as the scanning technology. The exclusive use of computed tomography (CT), rather than EBT, appears to be an attempt to lump and equate EBT and multislice CT under the same umbrella. EBT calcium scoring is supported by hundreds of peer-reviewed articles, including all of the authors’ references. Goldin et al3 recently demonstrated that helical CT is not a substitute for EBT and cannot be used as a surrogate for determining CCS. Until such time as CCS by multislice CT achieves the same scientific validation as EBT, we urge continued distinction between the technologies.

The authors conclude, “Participants without diabetes and those at intermediate risk may benefit from risk stratification based on high-sensitivity CRP levels and [coronary artery calcification].” This study’s cohort was at high risk, not intermediate risk. On the basis of Framingham risk estimates, the cohort (according to median values in Table 1 of the article1) had a 25% 10-year risk of hard cardiac events. Hecht, Rumberger, and Budoff use a specific brand of CT scanner (GE Imatron) and appear offended by unintended implications in our report. Our purpose was not to compare an inexpensive laboratory test with a costly radiographic measurement but rather to report that two manifestations of risk contribute independently to future heart disease. Coronary calcium is a surrogate marker, whereas CRP provides an assessment of atherosclerotic activity.

The specific criticisms:

Statistics. Our critics imply that our conclusions are based on “marginally significant results” relating CRP to future myocardial infarction coronary death (P=0.07 and 0.09). They overlook the additional significant (P<0.05) results:

- Significantly larger CRP values for those with end points (P=0.002).
- CRP was a significant predictor of any cardiovascular event (P=0.03).
- After adjusting for the risk factors and calcium, CRP still contributed to predicting any event (P=0.02).
- Compared with the low-risk CRP/calcium group, there was increasing risk for events with increasing CRP and calcium (P<0.001).

Furthermore, we are not changing our “predetermined level of significance” but rather using recommended procedures for reporting both statistically significant (P<0.05) and marginally significant (0.05<P<0.10) results. There is nothing “magical” about the cutoff of 0.05, and we are ethically responsible for reporting results that are close to the 0.05 level.

Scanner Brand. Hecht et al are concerned that we did not give sufficient recognition to the brand of CT scanner used in our study and in their commercial screening ventures (GE Imatron EBT). There are several scanner models available that produce results with calcium scores that have the same or improved accuracy when compared with the EBT brand.1–3 It would not be appropriate to name the brand of a diagnostic instrument every time we refer to it unless there is proof that a particular brand is superior to others. In this case, there is no such proof.

Intermediate Versus High Risk. Hecht et al imply that our results may not apply to adults at intermediate coronary heart disease risk. By substituting risk factor levels measured in our cohort into the Framingham risk algorithm,4 we find the mean 10-year coronary heart disease risk to be 19.8% at baseline, which is within the intermediate risk definition according to the National Cholesterol Education Program.2 We therefore stand by our characterization of this cohort as “intermediate” in risk.

Drs Hecht, Rumberger, and Budoff serve on the Speaker’s Bureau of GE-Imatron, South San Francisco, Calif.

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Reply

We reported that coronary calcium and C-reactive protein (CRP) contribute independently to predicting cardiovascular events. Hecht, Rumberger, and Budoff use a specific brand of CT scanner (GE Imatron) and appear offended by unintended implications in our report. Our purpose was not to compare an inexpensive laboratory test with a costly radiographic measurement but rather to report that two manifestations of risk contribute independently to future heart disease. Coronary calcium is a surrogate marker, whereas CRP provides an assessment of atherosclerotic activity.

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