Gender Differences Between High-Sensitivity C-Reactive Protein and Intima Media Thickness Progression

To the Editor:

Sander et al.1 have performed an excellent study demonstrating a significant sex difference in early atherosclerotic progression using high-sensitivity C-reactive protein (hsCRP). They have also showed that hsCRP failed to be associated with intima media thickness (IMT) progression, whereas in women, a significant association between IMT progression and hsCRP remained, even after adjustment for risk factors including statin treatment and HRT.

Two decades ago, 246 risk factors for coronary heart disease (CHD) had already been identified, and the number now continues to grow.2 High-sensitivity tests for CRP now make possible the measurement of CRP levels within the normal range.3 CRP is not only a marker of low-grade chronic systemic inflammation but also may be directly involved in atherosclerosis; it can amplify the inflammatory response through complement activation, tissue damage, and activation of endothelial cells.4 The binding of CRP to its ligands can activate the complement system, leading to the deposition of C3 in tissues. In animal models of myocardial infarction, this can lead to an increased area of infarction.5 The deposition of C3 and the activation of complement in arteries could potentially promote atherogenesis. A variety of in vitro studies suggest the existence of additional mechanisms of atherogenesis. CRP binds phosphocholine moieties such as those presented by oxidized phospholipids in LDL by promoting the uptake of LDL and the formation of foam cells.6 CRP can also promote endothelial activation and impair the production of nitric oxide.

But why does CRP remain a better predictor of CVD in women than in men? The question still remains unanswered and many have proposed reasons for this. Data from the Women’s Health Study7 conducted with a small case-control analysis with 3 years of follow-up showed that CRP levels predicted the risk of cardiovascular disease. Ridker et al.8 demonstrated that CRP is an independent predictor of cardiovascular disease. Their study included data from the entire study cohort of nearly 28,000 women with data on baseline levels of CRP, who were followed for a mean of 8 years, and used a composite cardiovascular end point.

Adiposity was a significant predictor of plasma CRP in postmenopausal women on a cross-sectional basis. Moreover, caloric restriction-induced weight loss decreased plasma CRP levels. Weight loss may represent an important intervention to reduce CRP levels, which may mediate part of its cardioprotective effects in obese postmenopausal women.9 Additionally, the metabolic syndrome is a stronger risk factor for early carotid atherosclerosis in women and it is an independent risk factor for early carotid atherosclerosis in women only.10 A prospective study by Tzoulaki et al showed that CRP was a significant predictor of lower-extremity atherosclerotic progression measured by ankle brachial index over 12 years of follow-up independently of cardiovascular risk factors.11 We need further prospective studies to identify the reasons for this gender difference.

Disclosures

None.

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