Reader's Comment on Meta-analysis of C-Reactive Protein and Risk of Angina Pectoris

The meta-analysis by Ruo-fei, et al indicated that an elevated levels of C-reactive protein (CRP) were associated with angina pectoris (AP), especially unstable AP, and were probably a risk factor of major adverse cardiac events.[1] Also, it highlighted that patients with AP syndromes can probably be prediagnosed by their plasma CRP levels.[1]

Measurement of CRP levels using high sensitivity assay (hs-CRP) can reveal subclinical inflammatory states, which may suggest existing vascular inflammation and consequently plaque vulnerability.[2] Therefore, elevated CRP is accepted as an independent predictor of future cardiovascular (CV) events, linear across a full range of values even beyond the ranges suggested by the CDC/AHA guidelines.[2] However, the CRP testing is not specific for coronary atherosclerosis and inflammatory cascade may have other initiators (e.g., systemic inflammation, local infections, and malignancies). In this context and based on the clinical data, detection of markedly elevated hs-CRP levels (≥10 mg/L), before being considered a false-positive test, may also suggest that chronic inflammation of alternate causes is responsible for increased CV risks.

In a study published in 2009, we demonstrated that higher hs-CRP levels in chronic coronary artery disease (CAD) patients may be independently associated with upper gastrointestinal lesions (UGIL), which were documented at endoscopy in almost 60% of our CAD patients chronically taking antiplatelet therapy.[3] Multivariate analysis (which included age, gender, smoking, hypertension, diabetes mellitus, hypercholesterolemia, obesity, medication used, CAD severity estimated using Gensini score and *Helicobacter pylori* status) revealed independent correlation between UGIL and hs-CRP values, especially for values ≥6.1 mg/l. Also, there was a strong correlation between CRP levels and severity of UGIL, with decreasing CRP levels after endoscopically confirmed UGIL healing. The later might explain previously observed association between UGIL (as a cause of chronic low-grade inflammation) and atherosclerotic disease.[4,5]

Therefore, we would like to highlight that CRP is primarily an indicator of augmented inflammatory status, which is an active promotor of atherogenesis and trigger of acute coronary syndromes. Inflammatory process causing elevated CRP, even when primarily located outside of the CV system, can still promote atherosclerosis through a number of proatherogenic and prothrombotic mechanisms. Therefore, patients in whom elevated CRP indicates higher inflammatory risk also require very intensive management of CV status (e.g., intensification of statin therapy). In patients with very high hs-CRP levels (>10 mg/l), as was noted in some of the studies included in this meta-analysis, other causes of chronic systemic inflammation should be considered because their healing can additionally reduce systemic inflammatory risk, the progression of CAD and the onset of major adverse cardiac events.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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