High Sensitivity C-reactive protein and other markers of cardiovascular inflammation: from bench to prove of efficacy

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The interest of CRP in CHD arise from its long half life and the robustness and reliability of its assessment.To date, CRP is the inflammatory marker most extensively assessed in prognostic studies, both in primary and in secondary prevention, and the only one recommended in guidelines. More than 25 different prospective studies have reported a significant and independent association between increased concentrations of hs-CRP and future cardiovascular events in apparently healthy subjects. Increasing quartiles of hs-CRP are associated with an increasing risk of future CHD at up to 10 years follow-up in apparently healthy men and women, in elderly subjects (and, even more interestingly, hs-CRP may add important information to the Framingham risk score and to the family history in the population at intermediate risk, thus allowing an improved reclassification of these subjects in either high or low risk. Lastly, in the JUPITER trial, the statin-mediated reduction of the CRP levels in subjects with normal LDL-cholesterol levels (<130 mg/dl), not candidates for statin therapy on the basis of NCEP III guidelines, was associated with a lower incidence of cardiovacular events at two years follow-up.

In patients with NSTEACS, many large studies have confirmed an independent strong value of CRP in predicting the recurrence of cardiac events, such as death, myocardial infarction and need for coronary revascularization procedures. Strong data are available about the prognostic value of CRP in the mid to long term: they clearly show that CRP levels predict recurrence of cardiac events, especially death, for up to five years, either in medically and in surgically or invasively treated patients, in which pre-procedural CRP levels correlate with incidence of restenosis after stent implantation. Of note, CRP gives incremental information on top of the TIMI risk score and of other biomarkers as NT-proBNP and troponin.

To date, CRP is the only inflammatory biomarker currently recommended by NACB guidelines for risk assessment of patients with ACS (class IIa, level of evidence A).

Growing evidence suggests a role of CRP as therapeutic guide, both in patients with ACS and in healthy subjects, and, intriguingly, as direct therapeutic target. In patients with ACS, treatments associated with reduced mortality, such as aspirin, clopidogrel, Gp IIb/IIIa inhibitors, ACE inhibitors, ARBS and especially statins, are also associated with lowering of CRP and are most effective in patients with high CRP levels. So far, it has been clearly shown that the presence of elevated CRP levels (> 3 mg/L) at admission or their persistence after optimal revascularization demands an aggressive medical treatment, and the therapeutic goal of very low CRP levels seems very likely. Also in apparently healthy subjects, data from the AFCAPS/ TexCAPS and JUPITER trials suggest that CRP screening might be an effective method to identify subjects who are more or less likely to benefit from statin therapy for cardiovascular risk reduction, regardless of cholesterol levels.

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