

C-Reactive Protein and Atherothrombosis: Cause or Effect?

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Objectives:

The complex relationship between the inflammatory response and vascular injury and repair is of major importance to the pathogenesis of cardiovascular disease. CRP is not only a strong marker for cardiovascular morbidity but a modulator that suppresses local and systemic thromboregulatory pathways. The aim of the study was to elucidate whether CRP is involved in atherogenesis, in thrombosis, or in both components of the atherothrombotic process.

Methods and Results:

Using human CRP transgenic mice we showed that CRP increases thrombosis through several pathways including reduced nitric oxide production and activity and increased TP expression. CRP is produced mainly in the liver but, also in other organs such as the vasculature. We showed that local production of CRP by endothelial cells increases platelet adhesion to the endothelium in a p-selectin mediated pathway. Reducing CRP expression using SiRNA/CRP led to reduction in CRP and TP expression. Real time thrombus formation following photo-chemical injury was accelerated in CRPtg and delayed in CRPtgTp^{-/-}. Time until arterial occlusion was significantly shorter in CRPtg and prolonged in CRPtgTp^{-/-} as compared with controls (n=9-15, 35±3.4, 136±13.8 and 67±8.9 minutes respectively, p<0.05).

Conclusions:

While CRP is present in the atherosclerotic lesion, it is probably not pro-atherogenic and correlates only minimally with atherogenesis. Alas, CRP promotes thrombus formation and vascular occlusion. Thus, CRP is most likely not affecting atheroma build-up but rather the deleterious process of plaque vulnerability and thrombus formation.