**C-REACTIVE PROTEIN AND CORONARY VASOMOTOR REGULATION**

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C-reactive protein (CRP) is an acute-phase inflammatory marker. Recent evidence suggests that CRP may not only be an independent cardiovascular risk marker but also a mediator of inflammation and atherogenesis. However, the effect of CRP on coronary microvascular reactivity remains unknown. Herein, we assessed the action of CRP on coronary vasomotor function regulated by endothelial nitric oxide (NO) and arachidonic acid (AA)-prostanoid. Using videomicroscopic techniques, intraluminal treatment of isolated porcine coronary arterioles with a clinically relevant concentration of CRP (7 µg/ml; 1 hr) significantly attenuated the NO release and endothelium-dependent NO-mediated dilation to serotonin. In the presence of superoxide scavenger TEMPOL, NAD(P)H oxidase inhibitor apocynin, or p38 kinase (an upstream activator of NAD(P)H oxidase) inhibitor SB203850, the adverse effect of CRP on serotonin-induced dilation was prevented. CRP increased NAD(P)H oxidase activity and produced SB203850- and TEMPOL-sensitive superoxide production in the arteriolar endothelium. CRP also reduced AA-elicited endothelium-dependent dilation and PGI2 release and caused tyrosine nitration of PGI2-synthase (PGI2-S). Peroxynitrite scavenger urate failed to restore serotonin dilation, but preserved AA-stimulated PGI2 release/dilation and prevented PGI2-S nitration. NO synthase inhibitor and TEMPOL also protected AA-induced vasodilation. Collectively, CRP inhibits endothelium-dependent NO-mediated dilation in coronary arterioles by producing superoxide from NAD(P)H oxidase via p38 kinase activation. At resting state, the formation of peroxynitrite from superoxide and basal released NO compromises PGI2 synthesis by inhibiting PGI2-S activity through tyrosine nitration. By reducing NO bioavailability and impairing PGI2-S function, CRP could promote endothelial dysfunction and participate in the development of coronary artery disease.