Coagulation factor Xa stimulates interleukin-8 release in endothelial cells and mononuclear leukocytes: implications in acute myocardial infarction.

OBJECTIVE: In acute myocardial infarction (AMI), proinflammatory plasma C-reactive protein values are strongly associated with postinfarction morbidity and mortality. So far, the cause of these inflammatory changes is not well understood. Therefore, we sought to investigate the relationship between the activation of coagulation and subsequent systemic inflammatory changes in AMI.

METHODS AND RESULTS: Factor Xa (FXa) bound to tissue factor pathway inhibitor and prothrombin fragments F1+2 (F1+2) were used as a measure for activated coagulation. To assess systemic inflammatory changes, plasma interleukin (IL)-6 and IL-8 concentrations were analyzed by immunoassay. Blood samples were taken from 21 patients with AMI and 20 patients with stable angina pectoris. In AMI, tissue factor pathway inhibitor FXa but not F1+2 plasma levels were associated with circulating IL-8 (P=0.01). In vitro experiments revealed that FXa stimulated IL-8 and monocyte chemoattractant protein-1 release and RNA expression in endothelial cells and mononuclear leukocytes by activation of protease-activated receptor-1.

CONCLUSIONS: Our data suggest that coagulation FXa may contribute to proinflammatory changes in AMI by stimulation of IL-8 release. Therapeutic inhibition of the proinflammatory effects of FXa may improve the clinical course in AMI.
This study investigates the relationship between the activation of coagulation and systemic inflammatory changes in acute myocardial infarction. Tissue factor pathway inhibitor factor Xa but not F1+2 plasma levels were associated with circulating interleukin-8. In vitro factor Xa stimulated interleukin-8 and monocyte chemoattractant protein-1 release and RNA expression by activation of protease-activated receptor 1 as an underlying mechanism.