Abstract: P482

Markers of neutrophil extracellular traps are associated with adverse clinical outcome in patients with stable coronary artery disease

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Background/Introduction: Neutrophil extracellular traps (NETs), comprising nuclear content and granule proteins, are expelled from neutrophil granulocytes in a process termed NETosis, and are thought to play a central role in atherothrombosis.

Purpose: We investigated whether the circulating NETs markers, double-stranded DNA (dsDNA) and myeloperoxidase-DNA (MPO-DNA), are associated with future clinical outcome in patients with stable coronary artery disease (CAD).

Methods: Patients with angiographically verified stable CAD (n=1001) enrolled in the ASpirin non-responsiveness and Clinical Endpoints Trial (ASCET) were included. Follow-up was =2 years, recording 106 clinical endpoints (unstable angina, non-hemorrhagic stroke, myocardial infarction, or death). Blood samples collected at baseline were used to measure serum dsDNA and MPO-DNA using a fluorescent nucleic acid stain and ELISA, respectively.

Results: Significantly higher dsDNA levels (median (25th, 75th percentile)) were observed in the group reaching clinical endpoint as compared to those without (402 ng/ml (372, 447) vs. 393 ng/ml (359, 433), p = 0.019). Patients with dsDNA in the upper three quartiles versus the lowest quartile were more likely to suffer the clinical endpoint, also after adjusting for relevant covariates (OR 2.01, 95% CI [1.12, 3.58], p = 0.019). Levels of dsDNA correlated with neutrophil count, body mass index, LDL-cholesterol, and triglycerides (r = 0.11-0.26, p = 0.001 for all). Males, smokers, and patients with metabolic syndrome had significantly higher levels of dsDNA (p = 0.002 for all). The highest quartile of dsDNA was associated with elevated markers of hypercoagulability (prothrombin fragment 1+2, D-dimer, free and total tissue factor pathway inhibitor (p<0.001 for all)). The two NETs markers were only weakly inter-correlated (r = 0.103, p = 0.001), and no significant associations to clinical endpoints, cardiovascular risk factors or hypercoagulability were encountered for MPO-DNA levels.

Conclusions: DsDNA levels were significantly related to adverse clinical outcome after two years, as well as several cardiovascular risk factors. DsDNA levels associated significantly, although weakly with a procoagulant state, suggesting that the detrimental effects of NETs in CAD might extend beyond those related to hypercoagulability.