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# Neutrophil extracellular traps and heparin-induced antibodies contribute to vascular access thrombosis in hemodialysis patients

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**Objectives:** Anti-heparin/platelet factor 4 (PF4) antibodies may trigger severe thrombotic complications in hemodialysis (HD) patients. Tetrameric PF4 has a high affinity for extracellular DNA, which is a key component of neutrophil extracellular traps (NETs); therefore, the interactions between anti-heparin/PF4 antibodies and NETs can contribute to prothrombotic events. This prospective observational study included all incident and maintenance HD (MHD) patients.

**Methods:** Anti-heparin/PF4 antibody levels were measured by enzyme-linked immunosorbent assay; an optical density > 1.8 was regarded as clinically significant. In incident HD patients, we additionally measured serum nucleosome levels as representative markers of NETs, and the contribution of anti-heparin/PF4 and increased serum nucleosome levels to primary functional patency loss of vascular access was assessed.

**Results:** The frequency of anti-heparin/PF4 antibodies was significantly higher in incident HD patients compared to MHD patients (23.6% vs. 7.7%). Serum nucleosome level, as well as the WBC count, neutrophil count, and hs-CRP level, were significantly higher in anti-heparin/PF4 antibody-positive patients compared to the control. Platelet counts tended to be lower in the anti-heparin/PF4 >1.8 patients than controls. Relative risk calculations showed that the presence of anti-heparin/PF4 antibodies increased the risk of primary functional patency failure by 4.28-fold and this risk further increased with higher nucleosome levels. Furthermore, in the anti-heparin/PF4 antibody-positive group, the time to first vascular intervention was much shorter, and the risk of repeated intervention was higher compared to the controls.

**Conclusions:** In incident HD patients, the presence of anti-heparin/PF4 antibodies was associated with increased NET formation; this could be a strong predictor of vascular access complications.