

BLOOD COAGULATION ACROSS THE SPECTRUM OF CHRONIC KIDNEY DISEASE

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Statement of the purpose of the study: Cardiovascular disease (CVD) remains the leading killer of patients with CKD. The specific causes of the prothrombotic state in CKD patients remains elusive, and it is unclear whether clotting dynamics and platelet function differ across the spectrum of CKD, including HD and PD. This study evaluated the clotting processes across the entire CKD spectrum in order to identify future targets for investigation.

Statement of the methods used: This was a cross-sectional study of 85 subjects: 20 healthy volunteers, 20 CKD stages 3-5 (non-dialysis), 25 HD and 20 PD. Fibrinogen concentration, platelet aggregation (collagen-epinephrine closure time in seconds), platelet contractile force (PCF, platelet function), clot elastic modulus (CEM, clot stiffness) and thrombin generation were quantified.

Summary of the results: All CKD groups had significantly higher fibrinogen levels compared to controls ($p < 0.001$). Platelet aggregation was significantly longer in the HD group relative to the others ($p = 0.036$). PCF was highest in the pre-dialysis CKD and PD groups, relative to the HD and control groups (12.0 vs 8.0 Kdynes, respectively, $p < 0.001$). Similarly, clot stiffness was greater in the pre-dialysis CKD and PD groups, relative to the HD and control groups (CEM 49.0 vs 28.7 Kdynes/cm², $p < 0.001$). All CKD groups produced significantly less thrombin, and took significantly longer time to generate thrombin compared to controls (all p-values < 0.001).

Statement of the conclusions reached: The processes involved with clotting are not consistent across the spectrum of CKD. Pre-dialysis CKD and those receiving PD exhibit prothrombotic profiles. HD patients exhibited impaired platelet aggregation, platelet function, clot structure and thrombin generation despite having high fibrinogen levels. This may reflect a defect in fibrinogen-platelet binding in hemodialysis patients.