

Genetica, emostasi e trombosi

AN OBSERVATIONAL STUDY ON THE EFFECT OF HEMODIALYSIS MEMBRANES ON ENDOGENOUS THROMBIN POTENTIAL IN END STAGE RENAL DISEASE PATIENTS

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Background and Aims. Cardiovascular disease and thrombosis are the leading cause of death in chronic kidney disease (CKD) patients. The end stage renal disease patients undergoing hemodialysis (ESRD-HD) are predisposed to hemostatic dysfunction, also due to HD membrane bioincompatibility. In this study, we aimed to evaluate thrombin generation potential in patients at different stages of CKD, including ESRD-HD patients. Furthermore, in HD patients, we compared thrombin generation parameters in pre-hemodialysis (PRE-HD) vs. post-hemodialysis (POST-HD). We also focused on the impact of different HD membranes and vascular access on thrombin generation parameters in ESRD-HD patients.

Methods. In this prospective observational study, we recruited 61 patients at different stages of CKD: 31 patients at stages I to V and 30 at ESRD-HD; we also evaluated 6 healthy controls. Thrombin generation by calibrated automated thrombin assay was evaluated in different classes of CKD and ESRD-HD; then, thrombin generation as well as total extracellular vesicles (EVs), platelets, endothelium and leukocyte derived microparticles (MPs) by flow-cytometry were evaluated at PRE-HD and POST-HD in ESRD-HD patients.

Results. Patients with CKD stages III, IV, V and ESRD-HD patients exhibited significantly lower endogenous thrombin potential (ETP) than control group, suggesting a reducing trend in thrombin generation potential along with decreasing renal function. Moreover in ESRD-HD patients, a significant decrease in ETP (829.4±348.5 vs. 1083±342.7 nM•min; $p < 0.005$) and peak thrombin generation (185.5±84.14 vs. 257.7±55.40 nM; $p < 0.005$) together with a prolonged lag time (3.02±0.66 vs. 2.06±0.45 min; $p < 0.0001$) and time to peak (ttpeak) (5.86 ±1.57 vs. 4.25 ± 0.72 min; $p < 0.0001$) were observed at POST-HD compared to PRE-HD, indicating a lower thrombin generation potential after dialysis. The flow-cytometric analysis identified a clear split into two groups, with some patients showing a significant reduction in total EVs, platelets, endothelium and leukocyte derived MPs and activated platelets MPs at POST-HD compared with PRE-HD and others showing a significant increase at POST-HD than PRE-HD, suggesting the variation in clinical characteristics of the patients and types of HD membrane might affect the EVs release. At an exploratory analysis, we observed a significant reduction in ETP and thrombin peak, consistently with a prolonged lag time and ttpeak, in patients treated with polysulfone-based (PS) and polyethersulfone-based (PES) HD membranes at POST-HD than PRE-HD, whereas patients on heparin-coated acrylonitrile membrane (ACN) showed no significant difference in thrombin generation parameters between PRE-HD and POST-HD. ESRD-HD patients with arteriovenous fistula access showed significantly lower thrombin generation parameters at POST-HD than PRE-HD.

Conclusions. Overall, these findings indicate lower thrombin generation parameters in patients with ESRD-HD compared with other CKD groups suggesting a higher risk of bleeding of this population, particularly after HD, when thrombin generation further decreases. The alteration in thrombin generation potential in this population could be in part due to variation in HD membrane and vascular access type.

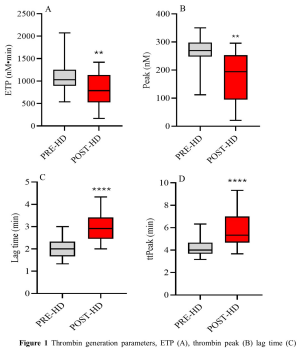


Figure 1 Thrombin generation parameters, ETP (A), thrombin peak (B) lag time (C) tPeak (D) in ESRD-HD patients at PRE-and POST-HD.** P < 0.005 and **** P < 0.0001 for POST-HD vs. PRE-HD.

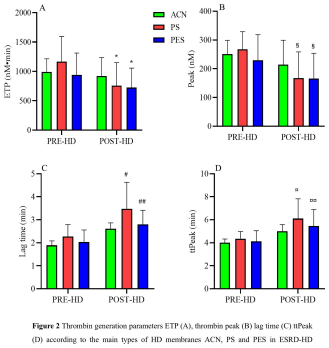


Figure 2 Thrombin generation parameters ETP (A), thrombin peak (B) lag time (C) tPeak (D) according to the main types of HD membranes ACN, PS and PES in ESRD-HD patients.* P < 0.05 for ETP, $ P < 0.05 for peak, # P < 0.05 and ## P < 0.005 for lag time and ¤ P < 0.05 and ¤¤ P < 0.005 for ttpeak of PS and PES at POST-HD vs. PRE-HD.