POI1798
Platelet Activity Mediates Enhanced Cardiovascular Risk in Patients with CKD and Peripheral Artery Disease
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Background: Chronic kidney disease (CKD) is common in patients with peripheral artery disease (PAD), and both are associated with poor cardiovascular (CV) outcomes. Platelets drive PAD pathogenesis and mediate atherothrombosis. Platelet function in CKD and the related CV risk is unclear. We investigated relationships between CKD, platelet activity, and incident CV events in a cohort of patients with PAD.

Methods: The Platelet Activity and Cardiovascular Events (PACE) study enrolled 289 patients with PAD undergoing lower extremity revascularization (LER). CKD was defined as eGFR<60 mL/min/1.73m² by the CKD-EPI equation. We measured platelet activity via light transmission aggregometry (LTA) in response to submaximal ADP, collagen, serotonin, epinephrine, and arachidonic acid (AA) prior to LER, and followed patients for a median of 18 months. The primary clinical endpoints were myocardial infarction (MI) and a composite of major adverse CV events (MACE; MI, stroke, death).

Results: There were 113 (40%) patients with and 172 (60%) without CKD. Patients with CKD (vs. non-CKD) were older and more likely to be female, Hispanic, have diabetes, heart failure, and critical limb ischemia (P<0.05 for each). There were no significant differences in prevalent coronary artery disease or use of antiplatelet therapy between groups. Platelet aggregation in response to submaximal ADP, serotonin, epinephrine, and AA was elevated in the CKD group (Figure). After multivariable adjustment, patients with CKD were at greater risk of MI (aHR 2.2 [95% CI, 1.02-4.9]; P=0.045) and MACE (1.9 [1.2-3.3]; P=0.01) than those without CKD. Platelet aggregation in response to submaximal agonist stimulation had a 25% and 12% mediating effect on the association of CKD with MI and MACE, respectively.

Conclusions: In patients with PAD, CKD was associated with increased platelet activity and CV events. Heightened platelet activity is an important mechanism underlying increased CV risk in CKD.

POI1799
Circulating Vascular Adhesion Protein-1 Level Predicts Risk of Cardiovascular Events and Mortality in Hemodialysis Patients
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Background: Vascular adhesion protein-1 (VAP-1) is an oxidative enzyme of primary amines that facilitates the transmigration of inflammatory cells. The oxidative and inflammatory effects of VAP-1 are prominently increased in pathological conditions such as metabolic, atherosclerotic, and cardiac diseases. However, the clinical significance of circulating VAP-1 levels in hemodialysis (HD) patients is unclear.

Methods: A total of 439 HD patients from the K-cohort were enrolled from June 2016 to April 2019. The plasma VAP-1 levels were measured at the time of study data entry, and the primary endpoint was defined as a composite of CV events and cardiac events in HD patients. The results of this study suggest the importance of future studies on the effect of VAP-1 inhibition in reducing CV events.

Conclusions: Plasma VAP-1 levels had the positive relationship with circulating levels of advanced glycation end-products and LV diastolic dysfunction. Higher VAP-1 levels were also associated with an increased risk of incident CV events and cardiac events in HD patients. Our results indicate that VAP-1 help clinicians identify those at high risk of CV events.

POI1800
Circulating Neprilysin Level Predicts the Risk of Cardiovascular Events in Hemodialysis Patients
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Background: Neprilysin inhibition has demonstrated impressive benefits in heart failure treatment, and is the current focus of interest in cardiovascular (CV) and kidney diseases. However, the role of circulating neprilysin as a biomarker for CV events is unclear in hemodialysis (HD) patients.

Methods: A total of 439 HD patients with the K-cohort were enrolled from June 2016 to April 2019. The plasma neprilysin level and echocardiographic findings at baseline were examined. The patients were prospectively followed up to assess the primary endpoint (composite of CV events and cardiac events).

Results: Plasma neprilysin level was positively correlated with left ventricular (LV) mass index, LV end-systolic volume, and LV end-diastolic volume. Multivariate linear regression analysis revealed that neprilysin level was negatively correlated with LV ejection fraction (β = -2.14, p = 0.013). The cumulative event rate of the composite of CV events was significantly greater in neprilysin tertile 3 (p = 0.049). Neprilysin tertile 3 was also associated with an increased cumulative event rate of cardiac events (p = 0.016). In Cox regression analysis, neprilysin tertile 3 was associated with a 2.61-fold risk for the composite of CV events (95% confidence interval [CI], 1.37–4.97) and a 2.72-fold risk for cardiac events (95% CI, 1.33–5.56) after adjustment for multiple variables.

Conclusions: Higher circulating neprilysin levels independently predicted the composite of CV events and cardiac events in HD patients. The results of this study suggest the importance of future studies on the effect of neprilysin inhibition in reducing CV events.

POI1801
Serum Cathepsin-S Concentration Is Not Related to Arterial Calcification Severity Among Hemodialysis Patients
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Background: Vascular calcification is prevalent among hemodialysis patients and is strongly correlated to their cardiovascular and total mortality. Cathepsin S, a lysosomal cysteine protease that is elevated in CKD patients, has shown its critical role of vascular calcification in cell culture experiments and in uremic animal model. To validate the relationship of Cathepsin S and vascular calcification in clinical practice, we conducted the current cross sectional study.

Methods: 88 patients on maintenance hemodialysis were enrolled and their serum Cathepsin S and its natural inhibitor Cystatin C were measured. Severity of vascular calcification was semi-quantified by aortic arch calcification (AAC) score on chest X-rays. Patients were divided into groups according to their AAC score, and the serum Cathepsin S level, Cathepsin S / Cystatin C ratio and other factors were compared between groups.

Results: There was no significant difference in the level of Cathepsin S (p=0.778) or Cathepsin S to Cystatin C ratio (p=0.417) between patients with different aortic arch calcification score. Only age was associated with the severity of AAC score (p=0.014).

Conclusions: Despite a pre-clinical study supporting the role of Cathepsin S in the development of vascular calcification under uremic and phosphate-rich conditions, serum Cathepsin S was not found to be associated with vascular calcification severity among hemodialysis patients in this study. Serum triglyceride is the strongest predicting factor for higher Cathepsin S levels in these patients. Further study is needed to confirm these findings using a different grading system.