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Abstract 1496: Protein Bound Homocitrulline Independently Predicts Mortality Risks in Maintenance Hemodialysis Patients

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Abstract
Background: Protein carbamylation increases during uremia. Recently we demonstrated that:

  i.   carbamylation is also catalyzed by myeloperoxidase;
  ii. occurs at sites of inflammation and in human atherosclerotic plaque;
  iii. confers multiple pro-atherosclerotic biological activities; and
  iv. plasma levels of protein bound carbamyllysine (homocitrulline) predict risk for major adverse cardiac events among subjects undergoing elective coronary angiography.

Herein we tested the hypothesis that homocitrulline levels predict adverse outcomes among subjects on maintenance hemodialysis (MHD).

Methods: Serum protein bound homocitrulline levels were quantified by tandem mass spectrometry in a cohort of MHD patients (N=347) with 5 yr follow-up.

Results: MHD patients who died (N=142) demonstrated higher protein bound homocitrulline levels than patients who are alive (N=205) (P=.02). Subjects with high (top tertile) levels of homocitrulline had increased all-cause mortality compared to those with low (bottom tertile) levels, with a 5 year hazard ratio for death of 2.7 (1.7– 4.3, 95% confidence interval), (P<.0001) following adjustment for sex, race, diabetes, history of cardiovascular disease, dialysis vintage, Charlson Comorbidity index, BUN, creatinine, IL6, albumin, and myeloperoxidase levels.

Conclusion: Serum levels of protein carbamylation are an independent predictor of mortality risk among MHD patients. Together these data suggest a mechanistic link between inflammation, uremia, and mortality among kidney failure patients.