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MATRIX GLA PROTEIN AND PREMATURE VASCULAR CALCIFICATION IN PATIENTS WITH END-STAGE RENAL DISEASE

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Background and Aims: Vitamin K is a potential protective factor against premature vascular aging and vascular calcification (VC). Whether vitamin K supplement could halt VC progression in patients with end-stage renal disease (ESRD) is not clear, partially due to the heterogeneity of measurements of VC in different vascular sites. Here we investigated the associations between non-phosphorylated, uncarboxylated matrix-Gla protein (dp-ucMGP), a circulating marker of vitamin K insufficiency, and premature vascular aging phenotypes evaluated by coronary artery calcium (CAC) scoring, aortic valve calcium (AVC) scoring, and histology scoring of presence of media calcification in vascular biopsies in patients with ESRD.

Method: In this observational cohort study, 223 ESRD patients (median age 54 years, 68% males) comprising non-dialysis patients (n=109), prevalent peritoneal dialysis (PD, n=80, median dialysis vintage 11.6 months) and prevalent hemodialysis patients (HD, n=34, median dialysis vintage 12.0 months) underwent baseline measurements of plasma dp-ucMGP and scoring of CAC and AVC by computed tomography scan. Framingham risk score (FRS), inflammation and other relevant clinical and biochemical data were determined at baseline. In a sub-group of patients (n=94), scoring of media calcification by histology in epigastric artery biopsies was also performed.

Results: Plasma dp-ucMGP levels (median 1568 pmol/L) significantly correlated with age ($\rho=0.38$), presence of cardiovascular disease (CVD, $\rho=0.16$), triglycerides ($\rho=0.19$), FRS ($\rho=0.33$), high-sensitivity C-reactive protein (hsCRP; $\rho=0.35$), CAC score ($\rho=0.30$) and AVC score ($\rho=0.24$) but did not differ with regards to treatment modality (i.e. non-dialysis, PD and HD). In multivariate regression analyses, with adjustment for presence of CVD, FRS, hsCRP and triglycerides, increased dp-ucMGP levels were independently associated with increased CAC score (**coefficients** 0.12, $p=0.04$), but not with AVC score nor presence of media calcification in epigastric arteries.

Conclusion: Our data suggest that vitamin K insufficiency as indicated by increased dp-ucMGP levels associates with premature vascular calcification evaluated by CAC but not with AVC or media calcification assessed by histology. This discrepancy warrants further studies to explore the pathophysiological background between vitamin K metabolism and susceptibility of calcification in different vascular sites as well as the pattern of VC (i.e. intima and media calcification) within sites.