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Clinical significance of plasma matrix metalloproteinase-2 and matrix metalloproteinase-9 levels to assess the cardiovascular risk in hemodialysis patients

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Objectives: Matrix metalloproteinases (MMPs) are endopeptidases that control extracellular matrix synthesis and degradation. Two MMP subtypes, MMP-2 and MMP-9, are known to play important roles in the development and progression of cardiovascular (CV) disease, but its clinical relevance as predictors of cardiovascular events is unclear in hemodialysis patients.

Methods: We prospectively enrolled 435 patients undergoing maintenance hemodialysis from K-cohort between June 2016 and April 2019. Plasma MMP-2, MMP-9 levels, and several biomarkers were measured at the time of study data entry. Primary endpoint was defined as a composite of cardiovascular events.

Results: Plasma MMP-2 level were increased in patients with incident CV events than those without CV events, whereas plasma MMP-9 levels were not different between groups. MMP-2 levels were positively correlated with circulating cardiac markers including brain natriuretic peptides (BNP), N-terminal proBNP, and heart-type fatty acid binding protein. The cumulative event rate of the composite of CV events was significantly greater in patients with higher MMP-2 tertile 3 than in those with other MMP-2 tertile 1 (p = 0.015). MMP-2 tertile 3 was associated with a 2.77-fold higher risk of the composite of CV events (95% CI, 1.40–5.45) and 4.67-fold higher risk of cardiac events (95% CI, 2.06–10.56) after multivariable adjustments. However, plasma MMP-9 levels were not positively correlated with circulating cardiac markers, and not associated with risk of incident CV events.

Conclusions: Higher plasma MMP-2 levels, but not MMP-9 levels, had the positive relationship with circulating levels of cardiac pathology markers, and were associated with increased risks of incident CV events and cardiac events among hemodialysis patients