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Association between circulating ECM-associated molecules and cardiovascular outcomes in hemodialysis patients

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Objectives: The extracellular matrix (ECM) is a complex network of non-cellular components that provide structural support for the tissues. Circulating ECM-associated molecules are increased during cardiovascular (CV) remodeling process and can be potential biomarkers of adverse CV outcomes. However, their clinical significance in hemodialysis patients is unclear.

Methods: A total of 372 hemodialysis patients were enrolled from a prospective multicenter cohort study. We measured four plasma ECM-associated proteins: matrix metalloproteinase (MMP)-2, MMP-9, tenascin-C, and thrombospondin-2. The primary outcome was set as a composite of cardiac and noncardiac vascular events.

Results: Plasma MMP-2 levels were significantly higher in patients with future CV events than in those without (p = 0.004), while the others were not. All the measured molecules had significant correlations with NT-proBNP levels, but the correlation coefficient was most strong with plasma MMP-2 (Rho = 0.317, p < 0.001). In logistic regression analysis, elevated plasma MMP-2 levels were independently associated with LV diastolic dysfunction (adjusted odds ratio [OR] per standard deviation, 1.48; 95% confidence interval [CI], 1.05 – 2.08; p = 0.024). Cox regression analysis showed that plasma MMP-2 levels were associated with a 1.30-fold risk for the composite of CV events (per a standard deviation increase; 95% CI, 1.04 – 1.63; p = 0.022) after multivariable adjustments.

Conclusions: Plasma MMP-2 levels were independently associated with an increased risk of LV diastolic dysfunction and adverse CV outcomes in hemodialysis patients. Our results suggest that MMP-2 levels can be a useful biomarker in identifying hemodialysis patients at high risk of future CV events.

figure 1. Correlation of circulating ECM-associated molecules and cardiac biomarkers