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Circulating Neprilysin Level Predicts the Risk of Cardiovascular Events in Hemodialysis Patients

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Objectives: 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 from 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.