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Sustained Diastolic Dysfunction and the Risk of eGFR Decline in CKD Patients with the Pre-HFpEF Phenotype: Application of the Parametric G-Formula

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Objectives : Structural cardiac alterations, notably diastolic dysfunction(DD), frequently complicate chronic kidney disease(CKD). With the growing recognition of the cardiorenal burden, understanding the complex organ crosstalk between the heart and kidneys has become crucial. Although the pre-heart failure with preserved ejection fraction(HFpEF) phenotype is highly prevalent in CKD, the longitudinal impact of its core driver, sustained DD, on renal disease progression and survival requires further clarification.
Methods : In this retrospective cohort of 15,582 CKD patients with ejection fraction(EF) ≥50%, baseline was defined at the time of the first echocardiogram. DD was identified via comprehensive echocardiographic parameters (e.g., E/E', PASP, or LAVI) alongside natriuretic peptides or diagnostic codes. The primary exposure was defined as continuous DD over a 5-year period. To overcome the inherent limitations of standard statistical models in handling treatment-confounder feedback, we applied the parametric g-formula. This approach adjusted for dynamic exposures (DD status) and time-varying confounders, including longitudinal changes in serum creatinine, serum bicarbonate, and prescriptions of medications such as RAAS blockade, SGLT2 inhibitors, and diuretics. Primary and secondary outcomes were a ≥40% decline in estimated glomerular filtration rate(eGFR) and all-cause mortality, respectively.
Results : At baseline, 4,470 patients presented with DD, and 11,112 did not. Over a median follow-up of 49.00 months, sustained DD across 5 years showed an independent association with a ≥40% eGFR decline (RR 1.54; 95% CI 1.37-1.73) compared to the persistent absence of DD. The estimated risk for all-cause mortality trended higher but remained statistically inconclusive (RR 1.74; 95% CI 0.25-8.39).
Conclusions : In CKD patients with the pre-HFpEF phenotype, the presence and persistence of DD showed an independent association with an elevated risk of kidney function decline. These robust associations, estimated through the g-formula accounting for dynamic clinical feedback, underscore the critical need for integrated cardiorenal surveillance for this population.