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Proteinuria Severity and Kidney Function Trajectories in Patients with Advanced Chronic Kidney Disease: Insights from CRIC and KNOW-CKD Study

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Objectives : Proteinuria is a key determinant in staging chronic kidney disease (CKD). However, its role in predicting kidney function decline and estimating time to kidney failure in advanced CKD remains underexplored.

Methods : We analyzed 2,727 participants with estimated glomerular filtration rate (eGFR) 15–45mL/min/1.73 m2 without kidney replacement therapy (KRT) from the Chronic Renal Insufficiency Cohort (CRIC) study and the KoreaN Cohort Study for Outcome in Patients with Chronic Kidney Disease (KNOW-CKD). The main exposures were baseline and time-updated urine protein-to-creatinine ratio (UPCR). The primary outcome was CKD progression defined as 50% or more decline in eGFR from baseline measurement or the initiation of KRT. The secondary outcomes included eGFR slope (mL/min/1.73 m2/year) and time to kidney failure.

Results : During 17,069 person-years of follow-up (median 4.9 years), the primary outcome occurred in 1,474 participants (54.1%). Compared with UPCR <0.5 g/gCr, the hazard ratios (HRs) (95% CIs) for UPCR 0.5–1.0, 1.0–3.0, and ≥3.0 g/gCr were 2.08 (1.76–2.45), 3.05 (2.64–3.52), and 6.32 (5.24–7.61), respectively. This association was stronger in analysis with time-updated UPCR, with the corresponding HRs (95% CIs) of 2.58 (2.13–3.12), 5.61 (4.76–6.62), and 12.88 (10.58–15.67), respectively. In secondary analyses, the eGFR decline slopes across respective categories were -0.87 (-0.98 to -0.77), -2.32 (-2.56 to -2.07), -3.41 (-3.63 to -3.19), and -5.45 (-5.93 to -4.97) mL/min/1.73 m2 per year. Additionally, time to kidney failure (95% CIs) decreased progressively with increasing proteinuria categories, estimated at 27.7 (24.7–31.5), 9.5 (8.6–10.6), 5.9 (5.6–6.3), and 3.5 (3.2–3.9) years, respectively.

Conclusions : Higher UPCR was strongly associated with accelerated CKD progression and a shorter time to kidney failure in advanced CKD, underscoring the critical role of proteinuria reduction in slowing kidney function decline, even in later disease stages.