**Association between urinary free light chains and progression to end stage renal disease in chronic kidney disease**

**Background:** In chronic kidney disease (CKD), higher serum levels of polyclonal free light chains (FLC) are independently associated with a higher risk of progression to end-stage renal disease (ESRD). It has also been shown that urinary FLC concentration increases as estimated glomerular filtration rate (eGFR).

We assessed for the first time whether urinary FLCs are independently associated with risk of progression to end-stage renal disease (ESRD) in patients with CKD, and whether they improve upon an established model for risk stratification.

**Methods:** We measured urinary FLCs in 556 patients with non-dialysis CKD in a prospective cohort study. The association between urinary kappa/creatinine (KCR) and lambda/creatinine (LCR) ratios and progression to ESRD was assessed by competing-risks regression (to account for the competing risk of death), expressed as a subhazard ratio (SHR) with 95% confidence intervals. The change in C-statistic and integrated discrimination improvement were used to assess the incremental value of adding KCR or LCR to the Tangri kidney failure risk equation (KFRE) for the prediction of ESRD at two years.

**Results:** The cohort had a median age of 64 years, 63% were male, and 68% were of White ethnicity. Median eGFR was 25 mL/min/1.73m2 and median ACR was 28.1 mg/mmol. Median urinary KCR was 14.6 mg/mmol, median LCR was 2.1 mg/mmol, and they were both positively correlated with serum FLC and urinary ACR, and negatively correlated with eGFR.

During the median follow-up time of 51 months, 136 participants developed ESRD. Higher KCR and LCR were both associated with a significantly increased risk of ESRD, but these became non-significant after adjustment for eGFR and ACR. However, having a KCR or LCR > 75th centile remained independently associated with the risk of ESRD (SHR: KCR 1.74 [1.12-2.71], LCR 2.05 [1.26-3.33]) after adjustment for age, sex, ethnicity, renal diagnosis, blood pressure, eGFR, and ACR.

Neither KCR nor LCR as continuous or categorical variables provided incremental value when added to the KFRE for estimating risk of ESRD at two years.

**Conclusions:** Urinary FLCs have an association with progression to ESRD in patients with CKD which appears to be explained to a degree by their correlation with eGFR and ACR. Levels above the 75th centile do have an independent association with ESRD, but do not improve upon a current model for risk stratification.