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Urine amphiregulin is associated with kidney damages and kidney function deterioration

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Objectives: Kidney fibrosis is the final common pathway in chronic kidney disease (CKD) development. However, therapeutic targets to suppress kidney fibrosis are not yet sufficient. We investigated the role of amphiregulin (AREG), the potential fibrotic marker, in patients with glomerulopathy.

Methods: This prospective observational cohort study included patients undergoing renal biopsies from January 2016 to December 2019. We measured urine AREG levels by enzyme-linked immunosorbent assays. The primary outcome was an annual change in estimated glomerular filtration rate (eGFR). The difference in eGFR changes according to the urine AREG levels was calculated using multivariable linear mixed models.

Results: Of the 185 participants with a kidney biopsy, 173 were eligible for the urine AREG analyses. The log-transformed urine AREG levels in diabetic nephropathy (4.11 ± 0.95 pg/mg) were significantly higher than those in minimal change disease (2.76 ± 0.67 pg/mg, $p = 0.013$) and minor glomerular abnormalities (2.94 ± 0.77 pg/mg, $p = 0.011$). The more advanced the CKD grade was and the higher the proteinuria measured, the higher the urine AREG levels (p for trend <0.001). Urine AREG levels were also significantly correlated with the severity of interstitial fibrosis (p for trend = 0.016), tubular atrophy (p for trend = 0.002), segmental sclerosis (p for trend = 0.028), mesangial expansion (p for trend = 0.001), and arterial intimal thickening (p for trend = 0.004). When grouping the participants according to tertiles of urine AREG, the eGFR decline of the third tertile was more prominent compared to the first tertile, even after the adjustment (difference in eGFR change per year = -6.02 ml/min/1.73 m², $p = 0.002$).

Conclusions: Urine AREG reflected the severity of renal function, proteinuria, and kidney pathologic findings. Furthermore, urine AREG showed potential as a biomarker that predicts the deterioration of kidney function.

Temporal changes of estimated glomerular filtration rate according to tertiles of urine amphiregulin level