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Soluble klotho as a marker of renal fibrosis and podocyte injuries in human kidneys

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Objectives: Klotho deficiency is relevant to renal fibrosis and podocyte injury *in vivo* and *in vitro*. We examined whether histological findings of renal biopsy specimens were associated with the levels of soluble klotho in humans.

Methods: We investigated renal biopsy specimens of 67 patients and detailed microscopic findings were reviewed. Soluble serum/urinary klotho and urinary angiotensinogen were assessed by enzyme-linked immunosorbent assays, and tissue klotho expression was assessed by immunohistochemical staining.

Results: The median age of the study participants was 35.6 years. High serum klotho levels (≥14 pg/mL) were associated with decreased odds ratios (ORs) of interstitial fibrosis (OR = 0.019, P = 0.003) and segmental sclerosis (OR = 0.190, P = 0.022) in multivariable logistic regression analysis. Patients with a lower urinary klotho-to-creatinine ratio (UKCR) were significantly more likely to have diffuse foot process effacement (OR = 0.450, P = 0.010). The area under the receiver-operating characteristic curve (AUC) of serum klotho for predicting interstitial fibrosis was 0.920 (95% CI, 0.844–0.996), and the best cut-off value of serum klotho was 138.1 pg/mL. The AUC of UKCR for predicting diffuse foot process effacement was 0.754 (95% CI, 0.636–0.872), and the best cut-off value of UKCR was 96.7 pg/mgCr. Urinary angiotensinogen-to-creatinine ratio was not associated with serum klotho, UKCR, or any pathological finding.

Conclusions: Our data suggested that soluble serum and urinary klotho levels represent a potential biomarker to predict renal fibrosis and podocyte injury in humans.