Urinary Biomarkers of Tubular Injury with End Stage Renal Disease and Long-term Renal Replacement Therapy in Type 2 Diabetes Mellitus: A Prospective Cohort Study

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Background: Diabetic kidney disease (DKD) typically evolves over many years, while the diagnosis, evaluation, and treatment are based mainly on biomarkers to assess kidney function. New potential tubular biomarkers in DKD can improve risk stratification and prediction.

Objective: To evaluate tubular damage markers with the incident end stage renal disease (ESRD) and initiating long-term renal replacement therapy (RRT) in Type 2 diabetes.

Methods: A prospective cohort study was conducted. A total of 271 type 2 diabetic patients were followed up. The baseline values of urine Cystatin-C to creatinine ratio (UCYS) urine angiotensinogen to creatinine ratio (UANG), urine NGAL to creatinine ratio (UNGal), and urine KIM-1 to creatinine ratio (UKIM) were measured. The primary outcomes were the incident ESRD and initiating of long-term RRT.

Results: The median follow-up period was 40.5 months. Urine tubular biomarkers of UCYS, UANG, UNGAL and UKIM were significantly higher among patients with new onset of ESRD and initiating of long-term RRT. In univariate followed by multivariate COX proportional hazard regression analysis, the number of patients with progression to ESRD was higher among those in the highest quartiles of UCYS (HR 8.08, 95% CI, 1.71-38.11), UANG (HR 4.98, 95% CI, 1.35-18.37), and UNGAL (HR 17.48, 95% CI, 2.01-151.76) than those in the lowest quartiles. In addition, the highest quartile of UCYS, UANG, and UNGAL were associated with 6.7 to 12.9-fold increased risk of initiating long-term RRT when compared with the lowest quartile in adjusted models. No significant associations were observed for UKIM with ESRD and long-term RRT.

Conclusion: The study supported that type 2 diabetic patients with high levels of urine tubular biomarkers (Cystatin-C, angiotensinogen, KIM-1 and NGAL) have a more incidence of ESRD and initiating of long-term RRT. These tubular biomarkers may be independent predictors of renal progression in DKD.

Keywords: Urine biomarker, Diabetic nephropathy, Urine cystatin, Urine NGAL, Urine angiotensinogen, Urine KIM-1