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Urinary CXCL16 and endostatin as biomarkers of tubulointerstitial fibrosis and rapid renal progression in patients with biopsy-proven advanced diabetic kidney disease

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Objectives: Proteinuria had been known to be one of the most important predictors for the decline in renal function, especially in patients with early stages of diabetes mellitus (DM). However, changing paradigms of DKD necessitate to discover the novel biomarkers for the prediction of decline in renal function. The aim of this study was to identify potential urinary inflammatory biomarkers than can reflect intra-renal pathologic findings in patients with biopsy-proven DKD. We also evaluated the association of these urinary biomarkers with renal pathologic findings and the decline in renal function.

Methods: A total of 70 patients with biopsy-proven isolated DKD were selected. Pathologic findings of enrolled patients were obtained from review of medical record, and various urinary inflammatory cytokines and chemokines were measured by multiplex ELISA.

Results: Most enrolled patients showed moderate to severe renal dysfunction at the time of renal biopsy, with a mean eGFR of 36.1 ml/min/1.73m² and a mean urine PCR of 7.77 g/gCr. Pathologic analyses revealed that IFTA was the only feature which was significantly associated with residual renal function among diverse pathologic features of diabetic nephropathy. Among various urinary inflammatory markers, MCP-1, CXCL16, and endostatin were significantly elevated in patients with severe IFTA. The rate of reaching ESRD was significantly higher in patients with severe ITFA as well as increased levels of CXCL16, endostatin.

Conclusions: Our study demonstrated that urinary CXCL16 and endostatin were significantly associated with both annual decline in renal function and renal outcome.