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The tissue expressions of tubular injury markers, NGAL and KIM-1, are associated with the decline of estimated glomerular filtration rate slopes in diabetic nephropathy

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Background: The tubular injury may be important in the pathogenesis and progression of renal dysfunction in addition to glomerular damage in diabetic nephropathy (DN). This study was conducted to examine whether tubular expressions of neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) have an independent association with progression of DN.

Methods: We retrospectively collected the data of all patients with diabetes who underwent renal biopsy at Samsung Medical Center from January 2000 to December 2014 and were confirmed to have DN. After exclusion of patients with other coexisting renal disease based on pathologic findings, estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73m^2, 35 subjects were included in the analyses. Annual decrease of eGFR was calculated by linear regression analyses. We assessed tissue tubular expressions of NGAL and KIM-1 by immunohistochemistry.

Results: Urinary protein to creatinine ratio (PCR) was a major determinant of subsequent GFR decline slope. The expressions of NGAL and KIM-1 on tubular cell were correlated with eGFR slope ($P < 0.001$, $P = 0.001$, respectively) and those of KIM-1 were also correlated with proteinuria ($P = 0.001$). In multivariate analysis, tubular expressions of NGAL remained as an independent predictor of eGFR decline ($P = 0.011$). However, KIM-1 expression was dependent on urinary PCR.

Conclusion: Proximal tubular injury may be secondary to proteinuria and that distal tubular injury may play an independent role in the pathogenesis of DN. Further studies are needed to determine if distal tubular injury can be a therapeutic target in DN.

Keywords: Diabetic nephropathy, Estimated glomerular filtration rate, Kidney injury molecule-1, Neutrophil gelatinase-associated lipocalin, Protein to creatinine ratio