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Non-invasive biomarker using urinary exosome miRNA that reflects pathologic features of patients with diabetic kidney diseases

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Objectives: Diabetic kidney disease (DKD) is a leading cause of end-stage renal disease worldwide. Although histological severity of DKD is a well-established predictor of adverse renal outcomes, investigations on the identification of non-invasive biomarkers that can reflect intrarenal status are scarce. The aim of this study was to discover urinary exosomal miRNA biomarkers of DKD and to examine their associations with the degree of various pathologic injury scores.

Methods: We collected and analyzed urinary samples obtained from 120 patients with biopsy-proven DKD and 32 healthy controls. The candidate microRNAs of DKD were selected by the analysis of public datasets and microRNA databases (miRTarBase, TargetScan, microRNA). Exosome RNA was extracted from urine supernatant, and the levels of selected candidate microRNAs were measured by quantitative real-time polymerase chain reaction.

Results:

Mean estimated glomerular filtration rate and urinary protein-to-creatinine ratio of enrolled DKD patients were 43.8 mL/min/1.73 m^2 and 6.1 g/g creatinine, respectively. Upon the analysis of public dataset, we identified 11 candidate microRNAs for DKD, and the expression of nine miRNAs in the candidates were significantly higher in patients with DKD compared to controls. In particular, urinary exosomal hsa-miR-30a-5p and hsa-miR-30c-5p levels were positively associated with the degree of interstitial inflammation, and their combination could predict rapid progression to end-stage renal disease. There was no significant association between the remaining microRNAs and the degree of glomerular injury, tubulointerstitial fibrosis, or arteriosclerosis. Finally, we found significant correlation between urinary protein-to-creatinine ratio and the levels of urinary exosomal miR-98-5p.

Conclusions:

Urinary exosomal microRNAs could reflect the degree of intrarenal pathologic status in patients with diabetic kidney disease.