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Clinical implication of isolated sub-nephrotic proteinuria and role of renal biopsy

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Objectives: Renal biopsy is a gold standard method to diagnose proteinuric glomerular disease. However, it is still controversial whether or not to perform biopsy in who have sub-nephrotic proteinuria alone without microscopic hematuria. Here, we examined clinical implication of isolated sub-nephrotic proteinuria and role of renal biopsy.

Methods: This retrospective longitudinal study was conducted with 826 patients who had been performed renal biopsies in 9 hospitals from 2002 to 2017. Isolated sub-nephrotic proteinuria was defined as spot urine protein-to-creatinine ratio less than 3.5 g/g, estimate glomerular filtration rate (eGFR) ≥60 mL/min/1.73m^2, and absence of hematuria. Primary outcome was the development of end-stage renal disease (ESRD).

Results: Patients were categorized into the amount of proteinuria; mild (<1g/g, N=455) and moderate (1.0-3.5 g/g, N=371). The most common pathological diagnosis was IgA nephropathy in both mild (73.4%) and moderate (61.2%) proteinuria groups. The remaining included membranous nephropathy, focal segmental glomerulosclerosis, minimal change disease, etc. During the median follow-up of 6.0 years, only overall 8 patients had developed ESRD. However, cumulative incidence of ESRD was lower in patients with mild proteinuria (P = 0.009) than in those with moderate proteinuria. Progression from mild to moderate proteinuria within one year after biopsy was associated with higher risk of the occurrence of eGFR < 60 mL/min/1.73m^2, whereas regression from moderate to mild proteinuria showed comparable risk when compared to those with persistent mild proteinuria. In addition, risk of eGFR < 60 mL/min/1.73m^2 was comparable among the types of glomerular diseases.

Conclusions: Prognosis of isolated sub-nephrotic proteinuria was benign. However, risk of kidney function decline differed according to changes in proteinuria during the first year after biopsy. Therefore, it may be possible to delay renal biopsy until moderate proteinuria occurs.