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Glomerular disease

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Optimal Proteinuria Target in Patients with Glomerular Diseases

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Background: Glomerular disease is one of the leading causes of end-stage renal disease (ESRD). Proteinuria is the hallmark of glomerular disease and is a major determinant of developing adverse outcomes in chronic kidney disease. However, the optimal proteinuria target for renoprotection is not conclusive. Therefore, the aim of our study was to investigate the optimal level of proteinuria reduction to prevent the progression of kidney disease in various types of glomerular disease.

Methods: Using glomerular disease registry of Yonsei University Health System, we conducted a retrospective observational study in 696 patients who were diagnosed with primary glomerular disease by kidney biopsy between 2005 and 2013. Time-averaged proteinuria (TA-P) was calculated as the mean of every 3 month period of spot urine protein-to-creatinine ratio. Patients were divided into 4 groups according to TA-P; >1, 1-2, 2-3, and >3g/g. The study endpoint was a composite of a 50% decline in estimated glomerular filtration rate (eGFR) or the onset of ESRD.

Results: We analyzed 413 patients with IgA nephropathy, 141 with membranous nephropathy (MGN) and 142 with focal segmental glomerulosclerosis (FSGS). During a median follow-up duration of 61 (3.1-127.0) month, the composite outcome occurred in 44 (10.5%) patients with IgA nephropathy, 17 (12.1%) with MGN and 23 (16.2%) with FSGS. For IgA nephropathy, patients with TA-P < 1 g/g had the lowest risk of developing a 50% decline in eGFR or ESRD, as compared to patients with TA-P of > 1 g/g. Hazard ratios (HRs) for reaching the composite outcome were 6.38 [95% confidence interval (CI), 2.55-15.95; P<0.001], 19.79 (95% CI, 6.87-57.0; P<0.01), and 29.64 (95% CI, 10.29-85.30; P<0.01) in patients with TA-P of 1.0-2.0 g/g, 2.0-3.0 g/g, and > 3.0 g/g, respectively. For MGN, the composite outcome occurred in 1 (2.4%), 1 (3.2%), and 2 (6.9%) patients with TA-P of < 1.0, 1.0 to 2.0, and 2.0 to 3.0 g/g (P=NS between-group difference), as compared to 13 (33.3%) patients with TA-P > 3.0 g/g (HRs, 16.35; 95% CI, 19.99-134.43; P=0.009). In patients with FSGS, risk for the progression of kidney disease did not differ between TA-P of < 1.0 and 1.0 to 2.0 g/g, while it was markedly increased in TA-P of 2.0 to 3.0 (HRs, 16.85; 95% CI, 1.95-145.87; P=0.01) and > 3.0 g/g (HRs, 18.69; 95% CI, 2.26-154.39; P=0.007).

Conclusion: This study showed that risk reduction for kidney disease progression was well correlated with decreasing proteinuria in IgA nephropathy, while moderately increased amount of proteinuria was not associated with an increased risk in MGN and FSGS. Therefore, the optimal level of proteinuria reduction can be individualized depending on types of primary glomerular disease.

Keywords: Focal segmental glomerulosclerosis, IgA nephropathy, Membranous nephropathy, Proteinuria