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Temporal association of hematuria with adverse kidney outcome in IgA nephropathy

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Objectives: Gross hematuria is generally known as a good prognostic indicator in IgA nephropathy (IgAN). However, a recent Spanish study showed that patients with persistent hematuria had higher risk of disease progression. Here, we comprehensively studied temporal association of hematuria with adverse kidney outcome in patients with IgA nephropathy.

Methods: Among 915 patients with biopsy-proven IgAN at Severance hospital between 2005 and 2017. The main exposures of interest were baseline and time-updated hematuria categorized as 0-5/HPF, 5-30/HPF, and ≥ 30 /HPF. The primary endpoint was a composite kidney outcome of a $\geq 30\%$ decline in estimated glomerular filtration rate GFR (eGFR) from the baseline value, or the onset of end-stage kidney disease. We used cause-specific hazard Cox models for hematuria and time-varying Cox models for time-updated hematuria.

Results: During a median follow-up of 19,702 person-years, the primary composite outcome occurred in 122 (13.3%) patients with the corresponding incidence rate of 6.19 [95% confidence interval [CI], 5.19-7.39] per 1,000 patient-years. In multivariable-adjusted cause-specific model, there was an inverse association of baseline hematuria with risk of CKD progression. Compared with urine RBC 0-5/HPF, the hazard ratios (HRs) (95% CI) for RBC 5-30/HPF and ≥ 30 /HPF were 0.3 (0.29-0.34) and 0.36 (0.34-0.38), respectively. There was a significant interaction between proteinuria and baseline hematuria for disease progression and the association of higher hematuria with lower risk of kidney outcome was particularly observed in patients with urine protein-to-creatinine ratio ≥ 1.0 g/g. However, this significant relationship disappeared in time-updated hematuria model. The corresponding HRs of urine RBC 5-30/HPF and RBC >30 /HPF compared with urine RBC of 0-4/HPF were 0.78 (0.47-1.29) and 0.80 (0.42-1.53), respectively.

Conclusions: In patients with IgAN, higher baseline urine RBCs was associated with lower risk of CKD progression. This association was lost in time-updated model, suggesting that its clinical significance become weak over time.