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Estimation of Single-Nephron Salt Excretion and Application to Clinical Nephrology

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Summary

Background/Aim: Kidney outcomes vary among patients with chronic kidney disease (CKD), but predictive factors for disease progression other than kidney function and proteinuria levels at diagnosis have not been established. Since the progression of CKD is defined by multiple factors including eating habits, it is desired to establish the indices that may better reflect the results of self-management by the patients. The kidney is responsible for most of the salt excretion, and it is known that excessive salt intake contributes to the blood pressure abnormalities and progression of CKD. We have recently developed a method for estimating the total number of nephrons in clinical settings (Sasaki T, Tsuboi N et al. Sci Rep. 2019). It is highly considered that he lower the number of nephrons in an individual, the higher the salt load to each nephron. Thus, we assumed that the amount of salt excreted per nephron may better predict the progression of CKD than total amount of urinary salt excretion. This study project aimed to examine the clinical significance of single-nephron urinary salt excretion (SNUSE), which was estimated based on the combined estimation of daily urinary salt excretion and total number of nephrons. Here, we report the results of analyses on the relationship between SNSUE and abnormality in blood pressure variabilities, which is one of the characteristics of CKD patients.

Methods: This study included biopsy-proven patients with IgA nephropathy (IgAN) diagnosed from 2010 to 2017. Kidney cortex volume was estimated from non-enhanced CT data and multiplied by volumetric glomerular density on kidney biopsy specimens to estimate the total number of nephrons. SNSUE was calculated by dividing the total daily urinary salt excretion by the total number of nephrons in both kidneys. The relationship between daytime and nighttime hypertension by ambulatory blood pressure monitoring (ABPM) was cross-sectionally investigated.

Results: The subjects were 178 IgAN patients (mean 42.5 years, 60% male, eGFR 60.4 mL/min/1.73 m^2). The total nephron number was estimated as mean 610,000/kidney, single-nephron GFR (SNGFR) was mean 46.2 nL/min, and single-nephron salt excretion (SNUSE) was median 5.7 μg/day. Patients with nighttime hypertension was associated with fewer number of nephrons. There was no difference in total salt excretion among the patients with and without daytime or nighttime hypertension, but SNUSE was higher in patients with nighttime hypertension. There was no difference in SNGFR among patients with and without daytime hypertension or nighttime hypertension. An increase in SNEUE was not observed in sub-group with nighttime hypertension treated with renin-angiotensin inhibitors.

Conclusion: These results suggest that the nighttime hypertension in IgAN patients associates with the compensatory increase in single-nephron salt excretion. The concept of SNUSE based on the individual number

of nephrons may be applied to optimize the salt intake for each patient. In order to generalize present results, we are planning to further analyze patients with kidney diseases other than IgAN.