Low serum chloride level gives renin-angiotensin system inhibitor a prognostic impact in heart failure patients with preserved ejection fraction

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Background: Hypochloremia is associated with a poor prognosis of heart failure (HF) patients. This phenomenon is sustained even in HF with preserved ejection fraction (HFpEF). Serum chloride level is known to be affected by serum renin secretion; however, this relationship is one of the least investigated field in HF patients. Renin-angiotensin system (RAS) inhibitor is recommended as a first-line medication for HF patients with reduced left ventricular ejection fraction, but no prior studies of RAS inhibitors have achieved to improve the prognosis of HFpEF patients.

Purpose: We investigated the relationship between baseline serum chloride level and the prognostic impact of RAS inhibitor in HFpEF patients.

Methods: This is an observational study including 1,913 consecutive patients who admitted to hospital due to worsening of HF and discharged alive in a single university hospital. After excluding patients who received regular hemodialysis and whose left ventricular ejection fraction were under 50%, 506 HFpEF patients were ultimately analyzed. They were categorized into tertiles by serum chloride levels at discharge (T1: –100 mEq/L, T2: 101–104 mEq/L, T3: 105- mEq/L), and patients in each category were further divided into subgroups depending on the prescription of RAS inhibitor at discharge (RAS inhibitor group and Non-RAS inhibitor group). The primary endpoint of this study was death from any cause.

Results: During the observation period with 479 days of median follow-up, 77 (15.2%) died. Patients in the RAS inhibitor group had significantly better prognosis than those in the Non-RAS inhibitor group in T1 category (Log-rank: p=0.003, Figure). In contrast, there was no statistical difference in the mortality between the RAS inhibitor group and Non-RAS inhibitor group in T2 and T3 categories (Log-rank: p=0.15, p=0.81, respectively, Figure). Multivariate Cox regression analysis in T1 category revealed that taking RAS inhibitor at discharge was independently associated with a lower mortality rate, even after the adjustment of diverse covariates (hazard ratio: 0.40, 95% confidence interval: 0.20–0.80).

Conclusion: In this observational study, the administration of RAS inhibitor was associated with an improved prognosis of HFpEF patients only in low serum chloride level at discharge. Therapeutic strategy focusing on the chloride level may be one of the promising options to find the light on a unintervenable prognosis of HFpEF.