



## Editorial

## With a grain of salt: Sodium levels in heart failure



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The clinical course of heart failure (HF) is often accompanied by electrolyte imbalances. Potassium and sodium levels are of special interest for clinicians as alterations may require immediate action to prevent harm. Hyponatremia is the most prevalent electrolyte disorder among hospitalized patients in general and frequently observed in both acute and chronic HF [1].

Low serum sodium levels in HF may result from multifactorial conditions (Fig. 1). A simplified approach distinguishes volume depletion from dilution. While the first is most commonly caused by diuretic, and hence saluretic, treatment such as loop diuretics or thiazides, the latter is characterized by an excess of water. This approach is simplifying a complex syndrome, however, it is useful in clinical practice since therapy strategies are diametrically opposed. In case of hyponatremia caused by depletion temporary discontinuation of diuretics and isotonic saline infusions often are sufficient for restoring the electrolyte balance and euolemia. Therapy in case of dilution is more complex. In the last few years, significant efforts have been undertaken to investigate whether pharmaceutical interventions for hyponatremia may improve outcome in HF. Hopes were pinned on vasopressin antagonists, leading to free water excretion, and therefore directly targeting dilutional hyponatremia. However, after conflicting data from several trials, the well-designed TACTICS-HF study recently demonstrated no effect of Tolvaptan in addition to standard furosemide treatment on the primary endpoint in patients with acute HF and a serum sodium value  $\leq 140$  mmol/L. Although Tolvaptan leads to an additional weight and fluid loss, the benefits of this treatment, also bearing its costs in mind, have to be scrutinized [2].

Still, treatment of hyponatremia in HF patients remains a challenge.

Hyponatremia has been linked with impaired prognosis in hospitalized patients in general [3], liver disease [4], and HF patients [5,6]. Most HF studies investigating hyponatremia focused on HF with reduced ejection fraction (HFrEF), however, in patients with

HF with preserved (HFpEF) similar results have been reported [7–10]. For mid-range ejection fraction HF (HFmrEF) data are scarce since this entity was introduced in 2016.

In this issue of the Journal, Imran and colleagues report on the impact of serial sodium measurements on outcome in patients with HFpEF. Investigating data of over 50,000 patients, they found a J-shaped association between serial serum sodium measurements and major adverse outcomes in these patients. The present study found that low serum sodium values at any point during follow-up represent a higher risk population. The authors conclude that serial measurements of sodium over time would be very important in identifying HFpEF patients at risk of adverse outcomes.

This is an important finding since most studies so far focused on one single serum sodium measurement. Given the dynamic nature of HF, serial measurements of any parameter of interest are highly desirable.

Registry data relying on standardized categorizations, like International Classification of Disease-9 as chosen in this study, allow for big data analysis (in the present study: >50,000 patients; >750,000 serum sodium measurements; >19,000 deaths) and are of immense importance. However, potential pitfalls have to be taken into account such as correct registration of co-morbidities. In the present study, atrial fibrillation was reported in 26.5% and a total of 2.0% were on aldosterone antagonist treatment, which is significantly lower compared to other HFpEF cohorts.

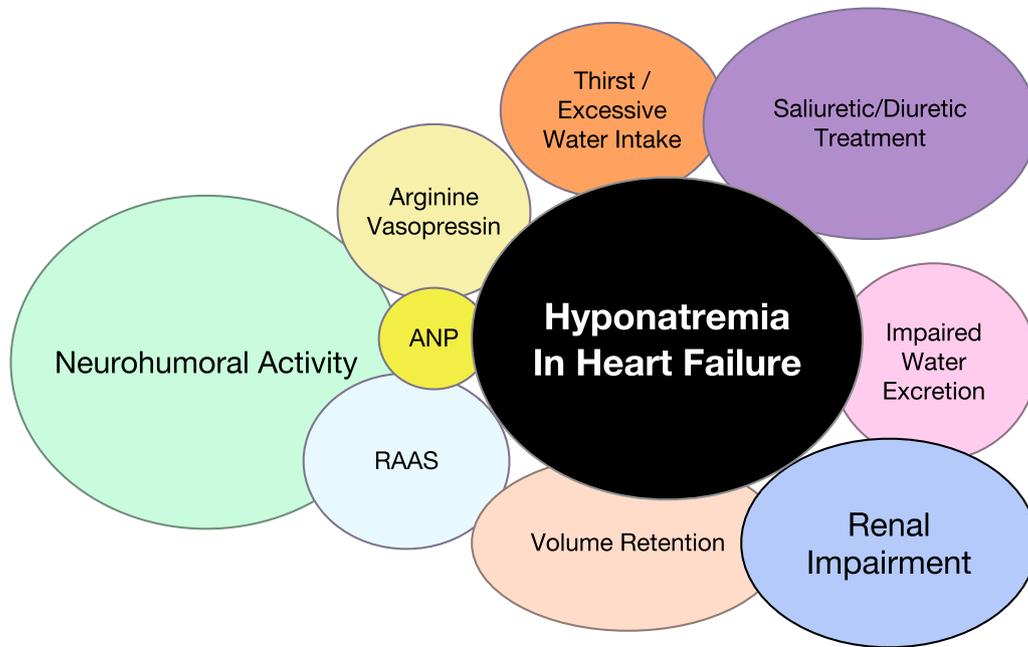
The present study adds important information in identifying risk factors in HFpEF. Despite significant efforts, no treatment option has yet been shown to improve prognosis convincingly in this high-risk population. Results from ongoing trials are eagerly anticipated in order to improve treatment options for these patients.

**Declaration of Competing Interest**

The authors report no relationships that could be construed as a conflict of interest.

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**Fig. 1.** Hyponatremia in heart failure represents a complex and multifactorial phenomenon. ANP indicates atrial natriuretic peptide; RAAS, renin–angiotensin–aldosterone system.

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