Rev Port Cardiol. 2017;36(7-8):521–523

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Serum sodium levels and blood pressure monitoring in heart failure: Added diagnostic and prognostic value☆

Natremia e medição de pressão arterial na insuficiência cardíaca: mais-valia diagnóstica e prognóstica

José Braz Nogueira

Faculdade de Medicina, Universidade de Lisboa, Centro Cardiovascular da Universidade de Lisboa, Lisboa, Portugal

Available online 14 July 2017

Hyponatremia is the electrolyte abnormality most often encountered in patients admitted for heart failure (HF).[1–3] Its prevalence ranges between 18 and 30%,[4–8] although it is lower in stable HF outpatients (10-17%).[9–12] It also varies with the severity and duration of HF, the criteria used to define it, medication prescribed and drug doses, particularly of diuretics. Most studies define hyponatremia as Na <135 mEq/l, although some use quartiles, and a linear relation has been observed between risk of short- and long-term total mortality and in-hospital cardiovascular morbidity and mortality and sodium <140 mEq/l. Other studies have demonstrated a U-curve for values between 140 and 145 mEq/l.[4–12] The value of natremia as a risk indicator is thus evident even for values considered normal; for every 3 mEq/l fall in blood sodium the risk of in-hospital mortality rises by 19.5% in HF with systolic dysfunction and by 8.6% in HF with preserved systolic function, and mortality 60-90 days after discharge rises by 10-18%.[4,5] Pathophysiologically, hyponatremia is multifactorial, usually due to hypervolemia related to hyperactivity of the sympathetic and rein-angiontensin-aldosterone systems and their effects on the kidneys. This hyperactivity is in turn secondary to reduced cardiac output and consequent reduced stimulation of aortic and carotid baroreceptors, which also induces an excessive increase in non-osmotic secretion of vasopressin and hence fluid retention.[1–3] However, diuretic therapy can transform this to normovolemia or even hypovolemia.[1–3] Recent reports suggest that chronic inflammation mediated by interleukin-6 may play a part in this increased vasopressin secretion.[13]

The relationship between blood pressure (BP) and HF, which may appear a simple one due to the known importance of high BP in the etiopathogenesis of HF, becomes more complex in light of the results of various studies that report worse prognosis in HF patients with lower office systolic BP, particularly below 120 mmHg, on admission, at discharge or even as outpatients, especially if they have reduced ejection fraction (EF).[14–17] A meta-analysis of 10 studies including over 8000 patients with stable chronic HF showed a reduction in mortality of 13% for every 10 mmHg higher systolic BP on admission.[17] However, some authors describe a U-shaped curve for long-term mortality with values between 120 and 139 mmHg, with slight differences between reduced and preserved EF.[15]

Most studies on the prognostic value of blood sodium levels in HF have shown that hyponatremia is associated with significantly lower office BP, which is also independently associated with higher risk.[4–12] The few studies on the prognostic value of ambulatory BP monitoring (ABPM) in HF show that non-dipper profiles (inverted dipper or riser) are more common in these patients, possibly related to increased sympathetic activity, and that these profiles are significantly associated with worse prognosis than for a dipper profile,[18–20] as has been shown in hypertensive patients and in population-based studies.[21,22] However, to the best of my knowledge no studies have set out to relate natremia lev-

☆ Please cite this article as: Braz Nogueira J. Natremia e medição de pressão arterial na insuficiência cardíaca: mais-valia diagnóstica e prognóstica. Rev Port Cardiol. 2017;36:521–523.

E-mail address: jnogueira@fm.ul.pt

els with BP values recorded by ABPM or with possible changes in circadian patterns.

The study by Arévalo-Lorido et al.[23] published in this issue of the *Journal* sets out to analyze precisely this relationship in 175 patients with stable HF, mostly of hypertensive etiology, assessed by ABPM. The authors found a significant correlation between serum sodium levels and systolic BP by ABPM in multivariate analysis, as well as a low prevalence of dipper pattern (20.5%), as has been reported both in patients hospitalized for acute HF and in those with stable chronic HF.[18–20] Furthermore, although they did not specifically examine the subgroup with Na <135 mEq/l, the usual definition of hyponatremia, they found that in the lowest quartile (133-139 mEq/l), both mean 24-hour and mean daytime systolic BP levels by ABPM were consistently lower than in the other quartiles. It should be noted that there were no significant differences in drugs prescribed in the different quartiles, including diuretics. There was also a lower prevalence of dipper pattern and a higher proportion of risers in the lowest quartile. Although, as pointed out above, non-dipper profiles are common in HF with either reduced or preserved EF, the riser pattern has recently been particularly strongly associated with HF with preserved EF and with increased risk.[19,20] In the present study, most patients in all quartiles of serum sodium levels had preserved EF, which may explain the high proportion of risers (38%), but this contrasts with the lower proportion seen in hypertension (5-19%).

The authors point out certain limitations of their study, including the fact that they were unable to form a true hyponatremic group, i.e. with sodium level <135 mEq/l (although several studies have shown increased risk with levels below 140 mEq/l[5,9,10]), and that they could not analyze HF with reduced and preserved EF separately, due to the preponderance of the latter, which could have further clarified some of the inter-relationships that have recently been reported, especially the increased risk seen in HF patients with riser profile and with preserved (but not reduced) EF.[20] Nevertheless, we consider their work to be original and of considerable interest, as it confirms the previously described association between low sodium levels and lower office BP in stable HF patients, only this time with 24-hour ABPM, with its added diagnostic and prognostic value. Furthermore, they raise the possibility that the changes in circadian profile found mostly in the lowest serum sodium quartile, particularly the lower prevalence of night-time dipping and the significantly higher proportion of riser profile, may improve risk stratification, higher risk being associated with lower sodium levels, as described in studies of both hospitalized[4–8] and outpatient[9–12] HF populations. The study may also contribute toward a better understanding of the pathophysiology involved, with specific serum sodium levels being used as markers or risk factors for overall mortality and cardiovascular morbidity and mortality in HF, and possibly as therapeutic targets.

Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Sica DA. Hyponatremia and heart failure – pathophysiology and implications. Congest Heart Fail. 2005;11:274–7.
2. Farmakis D, Filippatos G, Parissis J. Hyponatremia in heart failure. Heart Fail Rev. 2009;14:59–63.
3. Filippatos TD, Elisaf MS. Hyponatremia in patients with heart failure. World J Cardiol. 2013;5:317–28.
4. Klein L, O'Connor CM, Leimberger J, et al. Lower serum sodium is associated with increased short-term mortality in hospitalized patients with worsening heart failure: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study. Circulation. 2005;111:2454–60.
5. Gheorghiade M, Abraham WT, Albert NM, et al. Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry. Eur Heart J. 2007;28:980–8.
6. Gheorghiade M, Rossi JS, Cotts W, et al. Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the ESCAPE trial. Arch Intern Med. 2007;167:1998–2005.
7. Soto NS, Gheorghiade M, Kajimoto K, et al. Hyponatremia and in-hospital mortality in patients admitted for heart failure (from the ATTEND registry). Am J Cardiol. 2013;111:1019–25.
8. Lorido JCA, Gómez JC, Formiga F, et al. Hyponatremia as predictor of worse outcome in real world patients admitted with acute heart failure. Cardiol J. 2013;20:506–12.
9. Balling L, Schon M, Videboek L, et al. Prevalence and prognostic significance of hyponatremia in outpatients with chronic heart failure. Eur J Heart Fail. 2011;13:968–73.
10. Rusinaru D, Tribouillory C, Berry C, et al. Relationship of serum sodium concentration to mortality in a wide spectrum of heart failure patients with preserved and with reduced ejection fraction: an individual patient data meta-analysis. Eur Heart Fail. 2012;14:1139–46.
11. Bavishi C, Ather S, Bambhroliya A, et al. Prognostic significance of hyponatremia among ambulatory patients with heart failure and preserved and reduced ejection fractions. Am J Cardiol. 2014;13:1834–8.
12. Deubner N, Berliner D, Frey A, et al. Dysnatremia in heart failure. Eur J Heart Fail. 2012;14:1147–54.
13. Swart RM, Hoorn EJ, Betjes MG, et al. Hyponatremia and inflammation: the emerging role of interleukin-6 in osmoregulation. Nephron Physiol. 2011;118:45–51.
14. Gheorghiade M, Abraham WT, Albert NM, et al. Systolic blood pressure at admission, clinical characteristics and outcomes in patients hospitalized with acute heart failure. JAMA. 2006;296:2217–26.
15. Lee DS, Ghosh N, Floras JS, et al. Association of blood pressure at hospital discharge with mortality in patients diagnosed with heart failure. Circ Heart Fail. 2009;2:616–23.
16. Núñez J, Núñez E, Fonarow GC, et al. Differential prognostic effect of systolic blood pressure on mortality according to left-ventricular function in patients with acute heart failure. Eur J Heart Fail. 2010;12:38–44.
17. Raphael CE, Whinnett ZI, Davies JE, et al. Quantifying the paradoxical effect of higher systolic blood pressure on mortality in chronic heart failure. Heart. 2009;95:56–62.
18. Shin J, Kline S, Moore M, et al. Association of diurnal blood pressure pattern with risk of hospitalization or death in men with heart failure. J Cardiac Fail. 2007;13:656–62.
19. Komori T, Eguchi K, Saito T, et al. Riser pattern: another determinant of heart failure with preserved ejection fraction. J Clin Hypertens. 2016;18:994–9.

20. Komori T, Eguchi K, Saito T, et al. Riser pattern is a novel prediction of adverse events in heart failure patients with preserved ejection fraction. Circ J. 2017;81:220–6.
21. Fagard RH, Thijs L, Staessen JA, et al. Night-day blood pressure ratio and dipping pattern as predictors of death and cardiovascular events in hypertension. J Hum Hypertens. 2009;23:645–53.
22. Salles GF, Reboldi G, Fagard RH, et al. Prognostic effect of the nocturnal blood pressure fall in hypertensive patients – the Ambulatory Blood Pressure Collaboration in patients with Hypertension (ABC-H) meta-analysis. Hypertension. 2016;67:693–700.
23. Arévalo-Lorido JC, Carretero-Gómez J, Espinosa LM, et al. Ambulatory blood pressure monitoring in heart failure and serum sodium levels. Rev Port Cardiol. 2017;36:513–20.