Can Salt Sensitivity of Blood Pressure Be Assessed Without Changing Salt Diet?

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lood pressure is responsive to sodium intake in many patients with essential hypertension. It seems that subjects of African-American ancestry and older subjects are most sensitive to salt.1 Yet, there is no agreement on how such salt sensitivity is determined: frequently, such measurements involve 2 different periods on high- and low-sodium diets; others involve intravenous sodium loading and then low-salt diet and furosemide depletion. In different studies, the definition of salt sensitivity and related procedures differ substantially and quite arbitrarily (or perhaps empirically).1–3 Regardless of definition, in research settings salt loading or depletion is short term, while in reality, it is the long-term exposure that counts, especially with the recent recognition that sodium can accumulate in the skin and perhaps other tissues.4 Hypertensive subjects with salt sensitivity retain salt. However, salt retention also exists in other conditions. In renal failure, it is likely to be associated with hypertension, while not necessarily so in heart failure or cirrhosis of the liver. Healthy subjects with normal blood pressure may also be salt sensitive and are then more likely to become hypertensive over time.1

In individuals with salt-sensitive hypertension, high sodium intake expands vascular volume, and arterial pressure rises along with cardiac output. Urinary sodium excretion increases in parallel to blood pressure elevation, but balance is maintained at increased vascular pressures compared to salt-resistant normotensive subjects. Mechanisms of salt sensitivity are complex.1,4,5 They may include low birth weight with reduced nephron number, subtle renal injury and inflammation, nonmodulation of the renin-angiotensin-aldosterone axis and ouabain-like activity (Na+/K+-ATPase inhibition), changes in potassium intake, and expression of ion channels and supporting cellular skeleton, activation of macrophages by hypertonic interstitial environment, changes in nitric oxide signaling and presence of endogenous inhibitors, diminished atrial and other natriuretic peptides, aberrant renal prostanooid production, central activation of the sympathetic nervous system, among other candidates by the hyperinsulinemia frequently present in lean hypertensive sub-

jects, not to mention those with the metabolic syndrome, and are beyond the scope of our commentary.1–4

Salt sensitivity of blood pressure incorporates prognostic cardiovascular information, predicting target organ damage such as left ventricular hypertrophy, renal dysfunction, and increased risk of death,4 which may be independent of blood pressure, measured in the clinic.5 However, in numerous studies, salt sensitivity with high-salt diet were linked to higher nocturnal blood pressure (or lesser nighttime blood pressure decrease), recognizable only by ambulatory blood pressure monitoring1 (ABPM) and independently predicting adverse outcome in hypertensive patients.6 Thus, knowledge of a given patient’s salt sensitivity is important for diagnostic, prognostic, and therapeutic reasons. While decreasing sodium intake and diuretic therapy both reduce blood pressure, the magnitude and generality of the effect might be insufficient to ubiquitously recommend their adoption. A personalized recommendation based on measures of an individual’s salt sensitivity should, conceivably, prove more useful. As mentioned above, determining salt sensitivity is tedious, however, and primarily restricted to research settings.

In this issue of Hypertension, Castiglioni et al7 propose that a single ABPM session on usual diet can be used to predict a patient’s salt sensitivity. At first, this seems counterintuitive, because salt sensitivity is traditionally defined by repeated blood pressure measurements at low versus high sodium states. It is the practical complexity of such protocols at the clinical setting that motivated Castiglioni et al7 to search for surrogates of salt sensitivity within tracings of ABPM performed without controlling sodium diet. The richness of data embedded in ABPM seems to have provided them with candidates worthy of further study; the vast evidence linking nondipping of blood pressure during sleep,5 as well as their own previous observation on higher heart rate during the 24 hours of monitoring, led them to successfully combine both to indentify the majority, though not all, salt-sensitive patients based on “traditional” change from high- to low-salt diet (Figure). This approach is attractive and could be applied to epidemiological studies (to the extent such studies may successfully use 24-hour ABPM), as well as to individual patients who are more likely to willingly be so examined.

However, like in other cases, when the spectrum of diagnostics is broadened, new complications may arise: the fixed interval method of day and night definition for the purpose of calculating the nocturnal dip, which perhaps suits large epidemiological studies in some populations, may be plagued with behavioral problems when applied to individual subjects, and perhaps different populations. If patients sleep during daytime as is quite common in some Mediterranean countries, or if they get out of bed during the night as is not uncommon globe wide, the
resulting misclassification of daytime and nighttime blood pressure may have a devastating effect on the determination of the true sleep-related blood pressure dip. In addition, orthostatic hypotension, common among elderly hypertensive patients, is also associated with nondipping, or higher nocturnal blood pressure. Similarly, heightened sympathetic nervous system activity, common not only to salt-sensitive hypertension but also to renal failure, heart failure, cirrhosis of liver, as well as specific forms of secondary hypertension such as pheochromocytoma, may also be deceiving. Therefore, to be able to use the proposed new method, clinicians will have to exercise frequently under-used judgment and clinical skills rather than hook the patient to the monitor and let the data speak for itself.

Despite these reservations, the proposed categorization scheme appears to perform nicely when examining the original group of patients. As acknowledged by the authors, to further refine their suggested classification and provide direct applicability to clinical practice, one should next subject the chosen parameters (ie, dipping and heart rate) to more sophisticated statistical analyses to determine the most appropriate cutoff values. Alternatively, a continuous index might be derived from the product of the parameters to generate an “ambulatory sodium sensitivity index,” akin to the ambulatory arterial stiffness index and the blood pressure variability ratio, other cardiovascular physiology correlates derived from ABPM. Finally, consideration should be given to ABPM indices not examined in the current study. For example, sleep-related decrease in heart rate (the heart rate dip), an index associated with all-cause mortality, might be altered in salt-sensitive hypertension.

All these caveats considered, the elegant work of Castiglioni et al provides us with an exciting new opportunity to be able to identify many salt sensitive at hand and even retrospectively from existing databases.

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**References**

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