

HYPERTENSION

Urinary sodium and potassium excretion: association with blood pressure and clinical outcomes

Hypertension is an important modifiable risk factor for renal and cardiovascular disease and is reportedly associated with higher levels of sodium intake. New studies published in the *New England Journal of Medicine* provide further insight into the association between sodium intake, blood pressure, mortality and cardiovascular events. Together these studies reveal a positive but nonuniform association between sodium intake and blood pressure, and a J-shaped association between sodium intake and cardiovascular disease or death, with an increased risk of these adverse outcomes occurring in individuals with either high or low levels of sodium excretion.

Findings from previous studies have suggested an association between high levels of sodium intake and high blood pressure; however, this association has not been consistently observed and may differ between different populations and groups with different patient characteristics. To better understand the relationship between sodium intake and blood pressure, investigators of the large-scale Prospective Urban Rural Epidemiology (PURE) study examined the association of urine sodium and potassium excretion (as a surrogate of sodium and potassium intake) with blood pressure. 102,216 participants from 18 countries were included in the analysis.

After adjustment for covariates, the investigators found significant positive associations between estimated sodium excretion and systolic blood pressure, and between estimated sodium excretion and diastolic blood pressure, with increments of 2.11 mmHg in systolic blood pressure and 0.78 mmHg in diastolic blood pressure per gram increase in sodium excretion. The association between sodium excretion and blood pressure was evident across all geographic regions. Of note, the relationship between sodium excretion and systolic blood

pressure was nonlinear, with a steeper slope for the association at higher levels of sodium intake (increments of 2.58 mmHg in systolic blood pressure per gram for sodium excretion >5 g per day, 1.74 mmHg per gram for sodium excretion 3–5 g per day, and 0.74 mmHg per gram for sodium excretion <3 g per day; $P < 0.001$ for interaction). The researchers also noted an inverse association between estimated potassium excretion and systolic blood pressure, with each gram increment in estimated potassium excretion per day resulting in a 1.08 mmHg decrease in systolic blood pressure. The highest blood pressures were observed in individuals with the highest estimated sodium excretion combined with the lowest estimated potassium excretion. “These findings suggest that the effect of sodium on blood pressure is dependent on the background diet,” state the researchers.

To understand how patient characteristics might influence the association between sodium excretion and blood pressure, Andrew Mentz *et al.* performed a number of subgroup analyses. They found that the association between estimated sodium excretion and blood pressure was more pronounced in individuals with hypertension than in those without hypertension (increments of 2.49 mmHg in systolic pressure per gram versus 1.30 mmHg in systolic pressure per gram, respectively; $P < 0.001$ for interaction). They also found a significant trend according to age, with a steeper slope of association observed in individuals aged >55 years (2.97 mmHg in systolic pressure per gram) than in those aged 45–55 years (2.43 mmHg per gram) or those aged <45 years (1.96 mmHg per gram).

In a second study, the PURE investigators assessed the association between sodium excretion and death or cardiovascular events in 101,945 individuals. Over a mean follow-up of 3.7 years, the researchers found that



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compared with a reference level of estimated sodium excretion (4.00–5.99 g per day), higher sodium excretion (≥ 7 g per day) was associated with an increased risk of the primary composite outcome of death from any cause and major cardiovascular events (OR 1.15, 95% CI 1.02–1.30). Lower sodium excretion (<3 g per day) was also associated with increased risk of the primary composite outcome (OR 1.27, 95% CI 1.12–1.44). “Of note, the excess cardiovascular risk of high sodium intake (>6 g per day) was mostly observed in those with hypertension,” explains Mentz. “In addition, low sodium intake (<3 g per day) was not associated with lower cardiovascular risk compared to moderate sodium intake, despite lower blood pressure in these individuals.”

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Original articles Mentz, A. *et al.* Association of urinary sodium and potassium excretion with blood pressure. *N. Engl. J. Med.* doi:10.1056/NEJMoa1311989 | O'Donnell, M. *et al.* Urinary sodium and potassium excretion, mortality, and cardiovascular events. *N. Engl. J. Med.* doi:10.1056/NEJMoa1311889