

Natriuretic Response Prediction Equation Worth Its Weight in Salt?

By Nayan Arora

Law number 7 in the classic novel, *The House of God*, is age + blood urea nitrogen (BUN) equals Lasix dose (1). Limited data to guide diuretic therapy, the mainstay of treatment for patients admitted with decompensated heart failure, have given rise to similar urban legends uttered throughout hospital wards. Providers have traditionally relied on changes in weight and measurement of fluid intake and output for therapeutic decision-making. However, these variables can be notoriously difficult to obtain with accuracy and can result in therapeutic inertia, as data are collected within a 24-hour period. Furthermore, weight changes and fluid balance have shown considerable discrepancy and are not associated with 6-month survival (2, 3). Consequently, residual congestion is common and associated with adverse outcomes (4).

Whereas the aforementioned parameters are markers of total fluid balance, the variable of interest is natriuresis. Net negative sodium balance correlates with improved survival regardless of documented fluid balance. Negative sodium balance, even in patients with documented positive fluid balance, was associated with improved 6-month survival, whereas positive sodium balance was associated with worse survival, even among patients with negative fluid balance (3). Numerous studies have demonstrated the benefit of monitoring spot urine sodium values to gauge natriuretic response and allow rapid escalation of loop diuretics to achieve the desired therapeutic effect (5–10); however, measuring net sodium output remains challenging, as 24-hour urine collections on every hospitalized patient are neither feasible nor practical.

In the *Journal of the American College of Cardiology*, Rao et al. (11) proposed a natriuretic response prediction equation (NRPE), which utilizes a spot urine sodium 2 hours post-loop diuretic administration, along with glomerular filtration rate and serum/urine creatinine values to predict cumulative 6-hour natriuresis. This group previously demonstrated the ability of the NRPE to accurately predict cumulative sodium output with an area under the curve (AUC) of >0.9 compared with 6-hour urine collections (12). In this single-center study, the authors attempted to validate these findings in two cohorts: one to assess natriuretic response, categorized as poor, suboptimal, and excellent, defined as sodium output of <50 mmol, <100 mmol, and >150 mmol, respectively, and in the second, to utilize a nurse-driven protocol to guide loop diuretic titration using the NRPE among adult patients admitted with acute decompensated heart failure (ADHF). In 409 patients in the validation cohort, the authors again demonstrated excellent ability of the NRPE to predict a 6-hour natriuretic response with an AUC of 0.92 (95% confidence interval [CI], 0.89–0.95), 0.9 (95% CI, 0.87–0.93), and 0.9 (95% CI, 0.87–0.93) for a poor, suboptimal, and excellent response, respectively. The NRPE outperformed markers such as spot urine sodium concentration and net fluid output. Among 161 patients using the NRPE to guide diuretic therapy, significant improvement in net fluid output (–1.1 ± 0.9 L vs. –2.1 ± 0.9 L) and weight loss (–0.3 ± 0.3 kg vs –2.5 ± 0.3 kg) was seen after initiation.

An important limitation to the study is lack of information regarding validity in patients treated with continuous infusions of loop diuretics, as well as adjunctive agents, such as thiazide diuretics and acetazolamide, interventions that are common in hospitalized patients. Additionally, the protocol prioritizes maximizing loop diuretic therapy before consideration of adjunctive agents

for sequential nephron blockade, although it is currently unknown if one strategy is superior to the other. Nonetheless, this study provides a potential new tool to guide diuretic therapy among patients with ADHF. However, it would be prudent to demonstrate improvement in hard outcomes, such as rehospitalization, before widespread implementation. ■

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The author reports no conflicts of interest.

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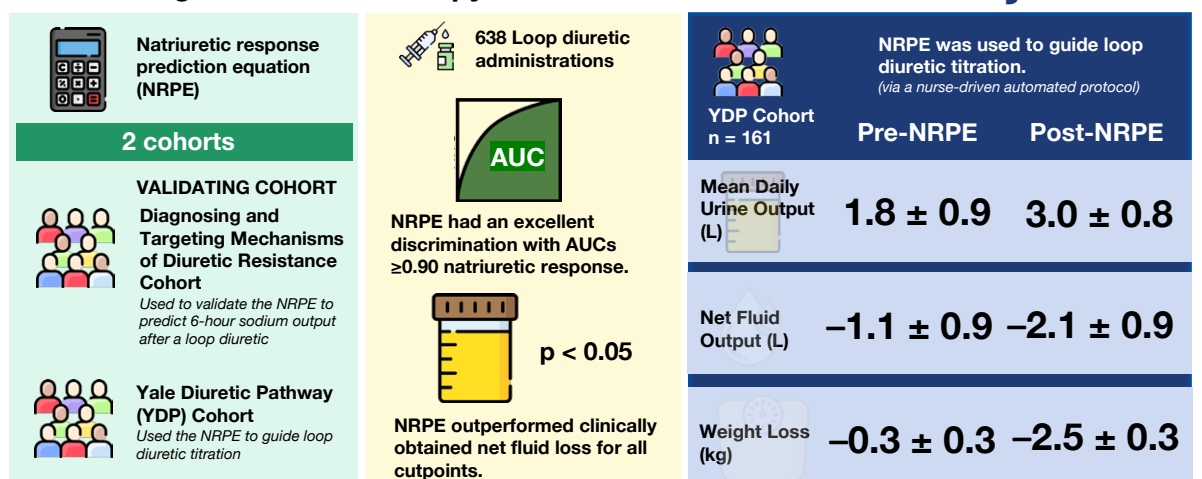
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Can the natriuretic response prediction equation be used to guide diuretic therapy?

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Visual Graphic by Edgar Lerma, MD, FASN