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## LETTER TO THE EDITOR

### Letter by Beldhuis et al Regarding Article, "Potential Role of Natriuretic Response to Furosemide Stress Test During Acute Heart Failure"

Iris E. Beldhuis, MD; Kevin Damman<sup>1</sup>, MD, PhD; Jozine M. ter Maaten<sup>2</sup>, MD, PhD

#### To the Editor:

We read with great interest the article "Potential role of natriuretic response to furosemide stress test during acute heart failure" of Dr Perez et al in which the authors study the role of natriuretic response to a furosemide stress test in patients with acute heart failure (AHF).<sup>1</sup> Although we fully endorse and advocate the importance of assessing (natriuretic) response to loop diuretic treatment in patients with AHF, we are hesitant regarding the use and terminology of a furosemide stress test in this context.

Traditionally, a furosemide stress test is used for predicting the progression to stage 3 acute kidney injury. Koyner et al<sup>2</sup> demonstrated that the 2-hour urine output after a standardized high-dose furosemide stress test in clinically euvolemic patients with early acute kidney injury has the predictive capacity of identifying those with severe and progressive acute kidney injury.<sup>2,3</sup> This is distinctly different from patients with AHF in which diuretics are the primary treatment for volume overload with the goal of achieving euvolemia, and as such assessing response is warranted to adequately adjust the decongestive treatment. In contrast, in the study of Perez et al, administration of furosemide is used to establish risk, and by using the term stress test, this further suggests that the response to furosemide (ie, diuresis and natriuresis) measures stress rather than response to therapy. To improve the treatment of patients with AHF, response to decongestive therapy and subsequent response guided therapy is recommended in a recent consensus paper on the use of diuretics.<sup>4</sup>

There are now several studies ongoing using natriuresis as response variable to guide loop diuretic treatment in AHF. In the ENACT-HF study (Efficacy of a Standardized Diuretic Protocol in Acute Heart Failure), a pragmatic, nonrandomized, multicenter, multinational study, natriuresis in the first hours after loop diuretic therapy will be used as response variable to guide treatment in the

first day, and compared with controls before the start of the protocol in the same center. In the PUSH-AHF study (Pragmatic Urinary Sodium-Based Treatment Algorithm in AHF), a randomized, single-center, controlled trial, natriuresis guided therapy will be compared with standard of care in AHF, with the co primary end point of 24-hour urinary sodium excretion, and the effect on first occurrence of all-cause mortality or HF hospitalization (URL: <https://www.clinicaltrials.gov>; Unique identifier: NCT04606927).<sup>5</sup>

Early assessment of natriuresis has been shown to be an accurate marker of insufficient diuretic response, as also illustrated by the findings of Perez et al, and could, therefore, be used to guide diuretic treatment, to improve decongestion and outcomes. The role of natriuresis guided therapy is in our opinion the most important next research question that should be answered in the treatment of patients with AHF. Indeed low natriuresis after loop diuretic therapy is a marker of risk, but it is important to characterize natriuresis as response variable, rather than designating it as a stress test.

Hopefully, the ongoing trials will provide more evidence in the near future to convincingly implement natriuresis as response variable in patients with AHF and improve decongestion and outcomes.

#### ARTICLE INFORMATION

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##### Disclosures

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