LETTER TO THE EDITOR

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

Pedro Caravaca Pérez[®], MD, PhD; Jorge Nuche[®], MD; Juan Carlos López-Azor[®], MD, PhD; Rafael Salguero-Bodes[®], MD; Fernando Arribas Ynsaurriaga, MD, PhD; Juan F. Delgado[®], MD, PhD

In Response:

We appreciate Dr Beldhuis et al¹ interest in our work and thank them for their enriching comments. We think that the questions raised are pertinent and allow us to explain our work in more detail.

We agree that the assessment of diuretic response, especially natriuresis, has become a fundamental element in decision-making and risk stratification in acute heart failure (AHF). Diuretics are not only the first-line treatment in AHF but can also be used for other purposes in this context. Furosemide's pharmacokinetic and pharmacodynamic characteristics make it an ideal tool to dynamically assess tubular integrity, which has proven helpful in different scenarios (acute renal failure, chronic kidney disease, and renal transplantation).²

Natriuresis is a useful biomarker in AHF with several applications including therapeutic-guidance (adjustment of diuretic treatment), prognosis assessment and risk stratification, and diagnostic value (tubular dysfunction).³ However, current studies on this subject suffer from a marked variability in the evaluation of natriuretic response to furosemide (different furosemide doses or the way of administration and timing for natriuresis quantification) making it difficult to compare studies and then generalize their results. Therefore, the furosemide stress test seeks to protocolize the assessment of natriuresis with a simple procedure, aiming to facilitate its translation to daily clinical practice. Thus, the furosemide stress test could be considered a diagnostic test for diuretic resistance by measuring patients' natriuretic response to controlled exposure to a prespecified dose of furosemide. The maximal natriuretic response evaluates tubular function and reserve, a recently described parameter that

seems to have a promising role for deepening cardiorenal interaction. In our humble opinion, the term furosemide stress test would be appropriate since it is a functional test assessing tubular reserve and diuretic resistance by administrating high doses of furosemide that stimulate active sodium secretion. Therefore, we propose using the furosemide stress test not only for guiding diuretic dosage but also to identify patients with diuretic resistance that could benefit from a more aggressive diuretic regimen since the first hours after admission.

As Beldhuis et al pointed out, the next challenge is to clarify whether natriuresis-guided diuretic treatment is actually a solid therapeutic target improving clinical events in AHF; or whether it is only a risk marker reflecting a more advanced stage of the disease.⁴

Although we understand that the semantic interpretation of the term stress test may generate controversy or give rise to different interpretations, we believe that both Dr Beldhuis and ours are complementary and value various aspects that enrich and emphasize the potential applications of natriuresis assessment in AHF.

ARTICLE INFORMATION

Affiliations

Servicio de Cardiología, Hospital Universitario 12 de Octubre, Madrid, Spain (P.C.P., J.N., J.C.L.-A., R.S.-B., F.A.Y., J.F.D.). Centro de Investigaciones Biomédicas En Red de enfermedades CardioVasculares, Madrid, Spain (P.C.P., J.N., J.C.L.-A., R.S.-B., F.A.Y., J.F.D.). Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain (J.N.). Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain (P.C.P., J.N., J.C.L.-A., R.S.-B., F.A.Y., J.F.D.). Facultad de Medicina, Universidad Complutense de Madrid, Spain (R.S.-B., F.A.Y., J.F.D.).

Disclosures

None.

For Disclosures, see page 112.

^{© 2021} American Heart Association, Inc.

Circulation: Heart Failure is available at www.ahajournals.org/journal/circheartfailure

REFERENCES

- Caravaca Pérez P, Nuche J, Morán Fernández L, Lora D, Blázquez-Bermejo Z, López-Azor JC, de Juan Bagudá J, García-Cosío Carmena MD, Escribano Subías P, Salguero-Bodes R, et al. Potential role of natriuretic response to furosemide stress test during acute heart failure. *Circ Heart Fail.* 2021;14:e008166. doi: 10.1161/CIRCHEARTFAILURE.120.008166
- McMahon BA, Chawla LS. The furosemide stress test: current use and future potential. *Ren Fail.* 2021;43:830–839. doi: 10.1080/0886022X. 2021.1906701
- Ronco C, Chawla LS. Glomerular and Tubular Kidney Stress Test: New Tools for a Deeper Evaluation of Kidney Function. *Nephron.* 2016;134:191–194. doi: 10.1159/000449235
- Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WHW, Orso F, Rossignol P, et al. The use of diuretics in heart failure with congestion - a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2019;21:137-155. doi: 10.1002/ ejhf.1369