

EDITORIAL

Abnormal renal function in acute heart failure: the same side of different coins

Disfunción renal en la insuficiencia cardiaca aguda: una misma cara de diferentes monedas

Enrique Santas¹, Julio Núñez^{1,2}

Renal failure (RF) is a common comorbidity in heart failure (HF), affecting nearly 50% of patients and is associated with an adverse prognosis¹. Of all the alterations in renal function that take place throughout the natural history of a patient with HF, one of the most important and controversial in clinical practice is the modification that occurs in the acute context of a HF decompensation, which has been defined as type 12 cardiorespiratory syndrome. Worsening of renal function (WRF) in acute HF (AHF) occurs in 20-40% of patients, and its incidence varies given the heterogeneity between the various patient profiles and the different definitions of WRF in the published series¹⁻³. The physiopathology of WRF in patients with AHF is complex, multifactorial and still largely unknown^{1,2}. Over the last decade, important developments have taken place in the knowledge of hemodynamic and neurohormonal factors linked to WRF in this specific clinical context. In this sense, and contrary to old postulates, current evidence shows that systemic venous congestion, and not renal hypoperfusion secondary to reduced cardiac output, is the main hemodynamic mechanism causally associated with its appearance^{1,2}. WRF in AHF has classically been associated with worse clinical outcomes and consequently its appearance leads to important diagnostic and therapeutic implications¹⁻³. However, recent studies point to a heterogeneous clinical significance resulting from its also diverse physiopathology. Generally, WRF has been associated with an increase in risk if the changes are of significant magnitude, they are sustained and coexist with data of poor clinical evolution and poor therapeutic response¹⁻³. On the contrary, discrete, transitory changes accompanied by good clinical and diuretic response in patients under vigorous diuretic treatment would not have any deleterious significance. The latter situation could be linked more to hemoconcentration and not to a true deterioration of renal function⁴.

In this issue of EMERGENCIAS, Llauger et al. present results of the EAFHE-EFRICA study, a secondary analysis of the EAHFE registry⁵. EAHFE is a prospective multicenter registry that over 6 recruitment phases, from 2007

to 2018, has included 18,370 consecutive patients with AHF in 45 Spanish hospital emergency departments (EDs). The authors deserve recognition for this hard work which has provided interesting information on the characteristics and prognosis of patients with AHF in the ED⁵⁻⁷.

In this study, the factors associated with the incidence of WRF in patients with AHF who attend the ED and its relationship with mortality are analyzed. It included 4,286 patients in whom serum creatinine was determined in 7 EDs in Spain. Of these, only 40% had their creatinine determined in the following 48 hours, with 1,627 patients finally included in the analysis⁵. This data should make us reflect, since in more than half of the patients there was no early determination of creatinine in the follow-up, despite the overwhelming evidence that we have on the importance of early assessment of renal function in patients with AHF. WRF was defined as the increase in creatinine ≥ 0.3 mg/dl at 48 hours, which is one of the most accepted definitions in the literature, although there is no universal consensus on this. In this case, it corresponds to grade 1 of the Kidney Disease Improving Global Outcomes (KDIGO)^{1,2} classification. The incidence of WRF was 13.5%, lower than that usually described in this context, which is 20-35%^{1,2}. Limiting its evaluation to the first 48 hours from the first medical care can probably explain the differences with earlier studies. Basal RF was the main variable associated with the appearance of WRF, in accordance with previous evidence^{1,2}. Patients with previous renal dysfunction are the most vulnerable to presenting WRF during an episode of AHF and it has a particular clinical impact on them^{8,9}. With regard to prognosis, the occurrence of WRF was significantly associated with an increased risk of mortality, which was of greater magnitude in the short term⁵. At 18 months of follow-up, the differences, although significant, were of lesser entity⁵. The results of this study deserve a series of considerations to be highlighted.

Firstly, it is important to emphasize the need for early assessment of kidney function in patients with AHF, given its important implications. This is important not only for patients who are hospitalized, but also for tho-

Author affiliation: ¹Cardiology Department, Hospital Clínico Universitario de Valencia, Universidad de Valencia, INCLIVA, Valencia, Spain. ²CIBER Cardiovascular, Valencia, Spain.

Contribution of the authors: The author has confirmed his authorship in the document of responsibilities of the author, agreement of publication and cession of rights to EMERGENCIAS.

Corresponding author: Julio Núñez. Cardiology Department. University Clinical Hospital of Valencia. University of Valencia. INCLIVA. Blasco Ibañez Avenue, 17. 46010 Valencia, Spain.

E-mail: yulnunez@gmail.com

Article information: Received: 12-5-2020. Accepted: 13-5-2020. Online: 20-5-2020.

Editor in charge: Óscar Miró.

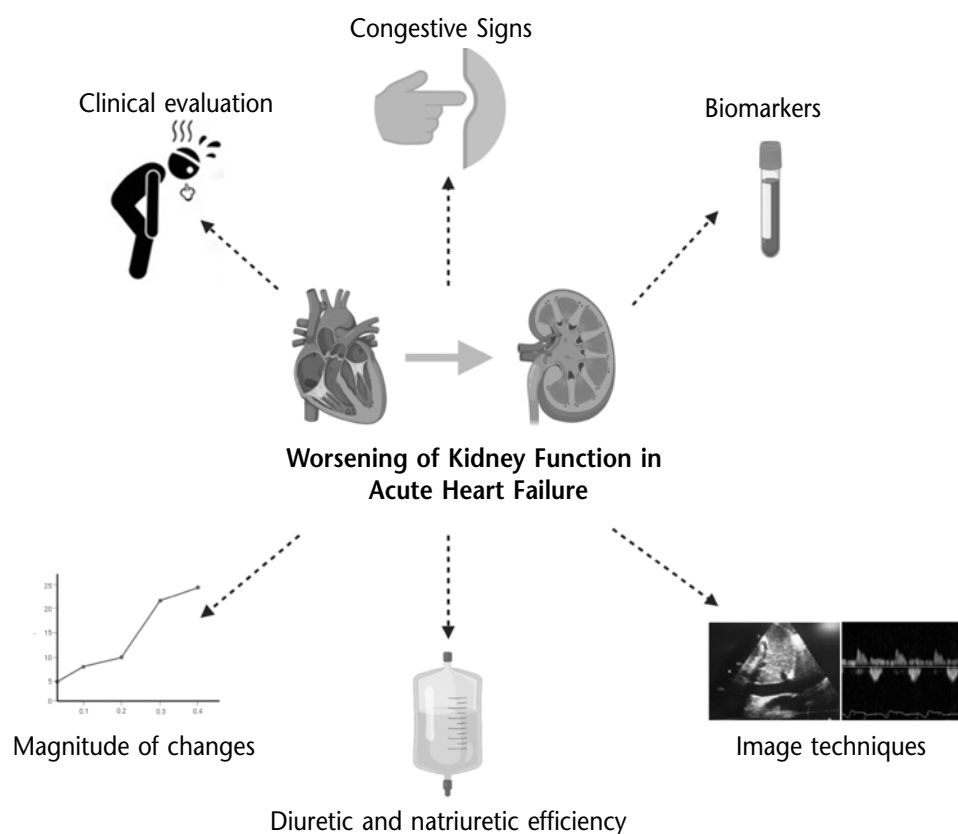


Figure 1. Important aspects to evaluate in clinical practice for an adequate interpretation of the worsening of renal function in acute heart failure.

se who are referred from the ED, where there should be a continuity of care that allows early transitional care. It is worrying that after a diagnosis of AHF a very relevant percentage of patients do not have short-term monitoring data of the renal function.

Secondly, although globally evaluated WRF is associated with a greater risk of death, its evaluation from the prognostic point of view should be considered according to the intensity of diuretic treatment, the degree of congestion and the clinical evolution during the first hours, which could allow us to better profile the different faces of this phenomenon^{1,2}. In this sense, different studies have shown that patients with WRF in the context of adequate decongestion and clinical improvement do not have an adverse prognosis. For example, in the DOSE clinical trial, a transient WRF in the context of intensive depletive therapy was associated with early clinical improvement, without worsening the prognosis at 60 days¹⁰. In a recent analysis of the AKINESIS study, WRF was only associated with an adverse prognosis if it was not accompanied by a decrease in natriuretic peptides¹¹. Adding more weight to this concept, an elegant recent study showed that in patients with adequate diuretic efficiency there was no relationship between WRF and elevated markers of renal tubular damage¹². Hence, future studies should ideally address the clinical significance and prognosis of WRF taking into account: a) the degree of congestion of the

patient, probably using biomarkers that are positively associated with surrogate congestion parameters, such as carbohydrate antigen 125^{13,14}, or imaging techniques that allow us to better quantify this phenomenon, such as evaluation of the inferior vena cava or renal venous flow by ultrasound¹⁵; b) surrogate markers of clinical evolution; c) the degree of diuretic/natriuretic efficiency; and d) new and more specific markers of renal injury, which allow us with greater profitability to differentiate true renal injury from that known as pseudoWRF^{1,2} (Figure 1).

In conclusion, the study by Llauger et al. confirms the importance of WRF in patients with AHF, reinforcing the concept of early assessment of kidney function after HF care in the ED. However, WRF in AHF is a complex phenomenon with different clinical significance depending on the magnitude of the changes, the clinical response, diuretics, hemodynamic and neurohormonal factors and the different effects of the treatments received. An isolated evaluation of serum creatinine is a simplistic approach to a multifactorial and complex phenomenon that almost always leads to clinical implications of diagnostic and therapeutic order that may not be the most appropriate.

Conflicting Interests: The author declares no conflict of interest in relation to this article.

Financing: The author declares the non-existence of financing in relation to this article.

Ethical responsibilities: The author has confirmed the maintenance of confidentiality and respect for patients' rights in the author's responsibilities document, publication agreement and assignment of rights to EMERGENCIAS.

Article commissioned and reviewed internally by the Editorial Committee.

References

- Mullens W, Damman K, Testani JM, Martens P, Mueller C, Lassus J, et al. Evaluation of kidney function throughout the heart failure trajectory- a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020;22:584-603.
- Núñez J, Miñana G, Santas E, Bertomeu-González V. Síndrome cardiorrenal en la insuficiencia cardíaca aguda: revisando paradigmas. *Rev Esp Cardiol*. 2015;68:426-35.
- Damman K, Valente MA, Voor AA, O'Connor CM, van Veldhuisen DJ, Hillege HL. Renal impairment, worsening renal function and outcome in patients with heart failure: an updated meta-analysis. *Eur Heart J*. 2014;35:455-69.
- Breidhardt T, Weidmann ZM, Twerenbold R, Gantenbein C, Stallone F, Rentsch K, et al. Impact of haemoconcentration during acute heart failure therapy on mortality and its relationship with worsening renal function. *Eur J Heart Fail*. 2017;19:226-36.
- Llauger LI, Jacob J, Moreno LA, Aguirre A, Martín-Mojarro E, et al. Factores asociados con el empeoramiento de la función renal durante un episodio de insuficiencia cardíaca aguda y su relación con la mortalidad a corto y largo plazo. Estudio EAHFE-EFRICA. *Emergencias*. 2020;32:332-9.
- Miró O, Gil V, Rosselló X, Martín-Sánchez FJ, Llorens P, Jacob J, et al. Patients with acute heart failure discharged from the emergency department and classified as low risk by the MEESSI score (multiple risk estimate based on the Spanish emergency department scale): prevalence of adverse events and predictability. *Emergencias*. 2019;31:5-14.
- Miró O, Martín-Sánchez FJ, Jacob J, Herrero-Puente P, Gil P, Llorens P. Pacientes en tratamiento con sacubitrilo-valsartán que presentan una descompensación en forma de insuficiencia cardíaca aguda: análisis de la actitud en urgencias y durante la hospitalización. *Emergencias*. 2019;31:407-12.
- Núñez J, García S, Núñez E, Bonanad C, Bodí V, Miñana G, et al. Early serum creatinine changes and outcomes in patients admitted for acute heart failure: the cardio-renal syndrome revisited. *Eur Heart J Acute Cardiovasc Care*. 2017;6:430-40.
- Núñez J, Llàcer P, García-Blas S, Bonanad C, Ventura S, Núñez JM, et al. A randomized controlled trial on carbohydrate antigen 125-guided diuretic treatment versus usual care in patients with acute heart failure. *Am J Med*. 2020;133:370-80.
- Felker GM, Lee KL, Bull DA, Redfield MM, Stevenson LW, Goldsmith SR, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med*. 2011;364:797-805.
- Wettersten N, Horiuchi Y, van Veldhuisen DJ, Mueller C, Filippatos G, Nowak R, et al. B-type natriuretic peptide trend predicts clinical significance of worsening renal function in acute heart failure. *Eur J Heart Fail*. 2019;21:1553-60.
- Ahmad T, Jackson K, Rao VS, Tang WHH, Brisco-Bacik MA, Chen HH, et al. Worsening renal function in patients with acute heart failure undergoing aggressive diuresis is not associated with tubular injury. *Circulation*. 2018;137:2016-28.
- Santas E, Palau P, Bayés-Genís A, Núñez J. The emerging role of carbohydrate antigen 125 in heart failure. *Biomark Med*. 2020;14:249-52.
- Núñez J, Bayés-Genís A, Revuelta-López E, ter Maaten JM, Miñana G, Barallat J, et al. Clinical role of CA125 in worsening heart failure: A BIOSTAT-CHF study subanalysis. *JACC Heart Fail*. 2020;8:386-97.
- De la Espriella-Juan R, Núñez E, Miñana G, Sanchis J, Bayés-Genís A, González J, et al. Intrarenal venous flow in cardiorenal syndrome: a shining light into the darkness. *ESC Heart Fail*. 2018;6:1173-5.