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Letters

TO THE EDITOR

Worsening Renal Function in Acute Decompensated Heart Failure

The Puzzle is Still Incomplete

We read with interest the article published by Salah et al. (1) in which they compared the prognostic meaning of plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) and creatinine changes in acute decompensated heart failure (ADHF). First, we would like to commend the authors for providing new valuable information aiming to unravel the clinical meaning of worsening renal failure (WRF) in ADHF. In this work, the authors found in a multicenter cohort of 1,232 patients admitted for ADHF that NT-proBNP changes during admission (a decrease higher than 30%), but not WRF, independently related to 180-day all-cause mortality and the composite of all-cause mortality and/or readmission for a cardiovascular reason (1).

These results are in agreement with recent reports in which WRF in ADHF patients lacked significant prognostic effect in a large spectrum of patients (2). WRF in ADHF is a final common pathway where several mechanisms and risk factors converge. This complex and multifactorial pathophysiology may explain why patients with WRF show mixed clinical response and outcomes (2). On one hand, WRF may be the mirror of low cardiac output and renal hypoperfusion, which lead to worse clinical outcomes (2); on the other hand, recent findings support that aggressive decongestion-mediated WRF may be also mirroring hemoconcentration, a condition associated to decongestion and clinical improvement (3).

In light of the current available knowledge, and to better understand the prognostic effect of renal kinetics in ADHF patients, we identify 3 scenarios that must be considered:

1. Clinical course and fluid overload status: A comprehensive approach, considering symptoms' evolution, vital signs, fluid overload surrogates, volume of diuresis, and, maybe, natriuretic changes is mandatory. Thus, WRF may be a proxy of hemoconcentration rather than true glomerular filtration impairment in congestive patients subjected to an aggressive depletive treatment and showing clinical improvement, adequate diuresis, and/or significant decrease of natriuretic peptides. In contrast, clinical awareness should be adopted in cases of coexistence of WRF with clinical deterioration, persistent hypotension, oliguria, and either no significant decrease or even increase of natriuretic peptides. Thus, and relative to the Salah et al. (1) data, we speculate a potential differential prognostic effect of WRF across NT-proBNP changes.
2. Baseline renal function and magnitude of changes: Recently, we reported that the clinical impact of ADHF renal function kinetics is largely determined by the presence of renal failure on admission and the magnitude of changes (4). Most creatinine changes are mild and lack significant prognostic effect in patients with normal renal function. It is very likely that in this subgroup of patients, WRF is just a surrogate of hemoconcentration as a result of decongestive treatment. Conversely, in patients with renal failure on admission, any increase in creatinine, even mild, was independently associated with a higher risk of 1-year mortality (4). In this scenario, and particularly in those with unequivocal fluid overload, an appropriate decongestive response would result in an improvement of renal function rather than WRF. Therefore, in this subset of patients, WRF might truly represent glomerular filtration rate, as a reflection, among others, of more severe illness, inappropriate aggressive decongestion, or even nonresponse to decongestive therapy.
3. WRF time of onset and duration: In contrast to persistent WRF, which is usually associated with hemodynamic derangements and higher risk of adverse outcomes, transient WRF as a result of aggressive decongestive therapy may not be associated with poor outcomes (5).

Finally, we would like to highlight that current WRF definitions have been validated mostly in non-heart failure scenarios (2). In absence of well-validated and widely accepted cutoff in ADHF, we believe evaluating the continuum of renal changes may provide more valuable information.

Acknowledging that several pieces are still missing to complete this difficult puzzle, current knowledge suggests that despite WRF in ADHF shares a similar

phenotype, it has very different underlying pathophysiological derangements and clinical meaning.

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REPLY: Worsening Renal Function in Acute Decompensated Heart Failure: The Puzzle is Still Incomplete

We thank Dr. Núñez and colleagues for their comments on our recent study on the competing risk between cardiac status and renal function during hospitalization for acute decompensated heart failure (HF) (1). We agree that there are different mechanisms for worsening renal function (WRF) during admissions for acute decompensated HF, and for that reason WRF in itself should not be looked on as a sole prognostic parameter but in relation to other prognostic parameters. Our study suggests that improving cardiac parameters (a sufficient N-terminal pro-B-type natriuretic peptide [NT-proBNP] reduction) outweighs WRF parameters. Indeed, others have also reported that WRF is outweighed as prognostic parameter when such parameters as hemoconcentration, weight change, and blood pressure reduction are considered. Unfortunately, these favorable parameters have not been compared with a natriuretic peptide response, but will probably indicate the same mechanism (i.e., that treating the effects of decongestion with success reflects the cardiac reserve). In addition to this, the *magnitude* of renal function change should be of primary interest, although it is not yet clear how this magnitude should be precisely defined. Nunez et al. (2) published on this topic recently where they described that even a mild loss of renal function was a prognostic adverse sign in patients with renal dysfunction already at baseline (estimated glomerular filtration rate, <60 ml/min/1.73 m^2). In contrast, loss of renal function was almost absent as a risk factor in patients with a normal baseline renal function (up to a change in creatinine of 0.8 mg/dl) (2). The distinction between these 2 groups was, however, a twice as high NT-proBNP level in patients with baseline renal dysfunction (estimated glomerular filtration rate, <60 ml/min/1.73 m^2), indicating a much higher "cardiac" risk in those with somewhat depressed renal function at baseline. Instead of pointing toward a certain renal mechanism of vulnerability, it may well suggest that in this particular subgroup the larger possibility to improve cardiac situation was important, rather than baseline kidney function. This idea was also confirmed by Testani et al. (3) in a recently published study, in which it was found that in the subgroup of patients with a baseline renal dysfunction primarily the BNP or the urea carries the prognostic information, and not the baseline renal function. In our study, only the more severe type WRF was found to be of importance for prognosis, defined as an absolute increase in serum creatinine level of >0.5 mg/dl in combination with >25% increase in serum creatinine level (1). So we would still advise to be aware of a *severe* WRF as it affects prognosis, and also attempt to find its causes, but accept a moderate WRF during hospitalization for acute decompensated HF and during therapies that aim to improve cardiac status. As a third comment, that is underlying this statement, and to further answer on the question of mechanisms of WRF, the renal function change and cardiac parameter change were dissociated in our study, as it was in other studies using BNP as a marker of cardiac status (4), or even with pulmonary artery catheter guidance toward lower left ventricle loading pressures (5). The incidence of renal dysfunction in our study was the same whether or not HF treatment was regarded as successful, and renal dysfunction was not prognostically worse between patients with or without a successful HF treatment in our study. This level of dissociation between cardiac and renal parameters may, to some extent, not in the extreme terms of cardiogenic shock,