Editorial

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Renal biomarkers in heart failure: an increasing need for sex-specific cardiovascular medicine.

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ABSTRACT

Heart failure exhibits high rehospitalization rates that compromise prognosis. Sex-stratified analysis of renal biomarkers and serum electrolytes emerges as an essential prognostic strategy. Recent evidence demonstrates that glomerular filtration rate predicts readmission in men, while serum calcium does so in women, with significant interactions between sex and creatinine/chloride. These findings underscore the need to abandon the "one-size-fits-all" approach in cardiology and develop sex-differentiated predictive models. Renal biomarkers, accessible and low-cost, offer opportunities for personalized risk stratification in post-discharge follow-up. Cardiovascular medicine must systematically incorporate biological sex perspective to optimize clinical outcomes.

Heart failure (HF) represents one of the most prevalent cardiovascular syndromes, with readmission rates reaching 50% within six months of hospital discharge. In this scenario, the article published in this issue provides relevant evidence on the prognostic usefulness of renal biomarkers and serum electrolytes, introducing a fundamental element: analysis differentiated by biological sex.

The authors, through an analysis of almost 2000 patients, show that renal biomarkers and measurement of serum electrolytes have a different prognostic value according to sex. This finding represent a call to drop the “one-size-fits-all” approach that is predominant in cardiology.

It is interesting to highlight in this publication, as in the male population, that a lower glomerular filtration rate (GFR) is significantly associated with a higher risk of readmission within six months; while in women, serum calcium emerges as the stronger predictor. This dichotomy suggests differentiated pathophysiological mechanisms, possibly reflecting different HF phenotypes, different neurohormonal responses, or mineral metabolism and renal function variations.

The association between lower GFR and greater risk in males reinforces the importance of cardiorenal syndrome. Renal dysfunction in HF is not just an epiphenomenon, but an independent predictor, reflecting the complex interaction between tissue perfusion, venous congestion, neurohormonal activation and pharmacological effects of fundamental therapies.

Calcium identification as a predictor exclusively in women raises questions about differentiated mechanisms. Could this be related to the bone mineral metabolism in post-menopausal women? Is there a relationship with HF phenotypes more prevalent in women, such as HF with preserved ejection fraction? Do hormonal changes influence calcium homeostasis and its myocardial impact? These questions deserve all our interest and further research.

Significant interactions between gender and biomarkers like creatinine and chloride add complexity to the analysis. Creatinine may be less sensitive in women due to less muscle mass, which may lead to renal dysfunction underestimation if not interpreted in an appropriate physiological context. The differential association of chloride underscores its underestimated role as prognostic marker, considering its participation in resistance to diuretics and acid-base balance.

These findings have immediate practical implications. We tend to apply the same risk algorithms regardless of sex. However, evidence suggests considering differentiated biomarkers panels, with adjusted thresholds and specific estimations according to the biological profile of the patient.

This study reminds us that biological differences between men and women with cardiovascular diseases are not minor, negligible variations. Women have been underrepresented for decades in most cardiovascular clinical trials, and rarely specific analysis are made with appropriate statistical power. This gap has led to a cardiovascular medicine mainly designed for men.

In Latin America, where HF prevalence is still increasing and there are limitations in resources, the identification of accessible prognostic biomarkers becomes particularly relevant. The evaluated markers are widely available, are a routine and do not require sophisticated technology.

We should be cautious when interpreting this study. The retrospective design and the absence of information on ejection fraction, functional class and treatment limit our understanding of the clinical context. The evaluated outcome corresponds to re-

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admissions by any cause, which may lead to a great heterogeneity at the time of analysis. Nonetheless, the study establishes the foundation for future research. Prospective, multicenter studies are required, including clinical, echocardiographic and therapeutic variables, validating these findings in diverse populations. It would be particularly important to explore whether these biomarkers in differentiated models do improve the identification of patients in high risk.

This study invites to systematically add the perspective of gender in cardiovascular research, from design to interpretation. The most recent guidelines have started to acknowledge these differences, but there is still a long way to go to achieve applicable recommendations.

To conclude, this study is a valuable contribution, reminding us that accurate medicine in cardiology should include the dimension of biological sex. Renal biomarkers and electrolytes, apparently simple tools, may provide differential prognostic information in an appropriate context.

As cardiologists, we should drop the "one-size-fits-all" paradigm and advance toward a truly personalized medicine, acknowledging the essential biological differences. Only thus we will be able to optimize the management of HF, readmissions will be reduced and prognosis and quality of life will improve, regardless of gender.

The challenge has been set. There is evidence. It is up to us to add it to our practice and to continue generating knowledge that would provide each patient with the best possible care, acknowledging their biological individuality as a crucial element in cardiovascular medicine.

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