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EDITORIAL COMMENT

Biomarkers in heart failure: A future or a long overdue promise?

Biomarcadores na insuficiência cardíaca: o futuro ou uma promessa adiada?

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Heart failure (HF) is a clinical syndrome that affects 1-2% of the adult population, with increasing prevalence with age (>10% in those aged 70 years or over). Although HF prognosis has improved due to new therapies, it is still a frequent cause for hospitalizations, with a major impact on health care resources. It can be due to several etiologies, but most commonly it derives from myocardial dysfunction.[1]

Heart failure impacts patients' quality of life, has an adverse prognosis and is a major cause of death and hospitalization. Following years of research, new advances in pharmacologic and device therapy have been achieved, optimizing patient care. Currently, one of the focuses of scientific research is on the role of biomarkers in diagnosis, therapy guidance and prognosis of HF. This was recently identified as a gap in evidence in the new European Society of Cardiology Heart Failure guidelines.[2] The search of a biomarker that could help identify patients at high-risk of adverse events and to alter patient management is one of the most sought after objectives in cardiology.

Segura-Saldaña et al.[2] aimed to observe the prognostic role of three biomarkers, red blood cell distribution width (RDW), high-sensitive C-reactive protein (hs-CRP) and interleukin-6 (IL-6) in patients hospitalized for acute HF. In their prospective study with a cohort of 167 non-ischemic HF patients, the authors concluded that IL-6 was an independent predictor of mortality when only considering age, gender and comorbidity confounders; however, its effect was not independent from most important clinical variables. Of the three biomarkers, IL-6 presented the best accuracy for mortality and RDW for severity.

The best cut-off value to predict mortality for IL-6 was 52.9 pg/mL (sensitivity 100%; specificity 75.35%; area under the curve (AUC) 0.91). As for severity, the best cut-off of RDW was 15.6% (sensitivity 93.6%; specificity 73.33%; AUC 0.87).

In recent years, several studies have addressed the impact of markers related to pro-inflammatory states, in an attempt to determine the prognosis of cardiovascular diseases. In HF, there are increased levels of circulating inflammatory cytokines and some studies suggest that they can predict clinical outcomes; hence, the interest in dosing and establishing a relationship between elevated inflammatory biomarkers and prognosis. Nonetheless, one should not forget that the concentration of these biomarkers increases with aging and in several chronic diseases (both characteristics present in several HF patients). Of note, the elevated concentration of inflammatory biomarkers can also be a consequence of HF (as a pro-inflammatory illness), and not the cause.

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High-sensitive CRP is one of the most widely studied biomarkers in several cardiovascular conditions. It is considered a marker of low-grade inflammation, even when there is only lminor CRP elevation. Its role in the assessment of cardiovascular risk is in continuous evolution.[3] In this study, hs-CRP was not an independent predictor of mortality, but it was associated with severity (after controlling for age, gender and comorbidities). However, the sensitivity of hs-CRP was considerably low, thus could limit its role in this clinical context.

Interleukin-6 is a pleiotropic cytokine that rises in response to injury. It activates immune cells and signal protective response, acting as an inflammatory mediator. Its elevation in HF has been previously recognized and is associated with a poorer clinical outcomes.[4] In this study, IL-6 presented the best accuracy for mortality and its effect on severity was independent from comorbidities, age and gender.

Red blood cell distribution width is a routinely assessed blood count component and is inexpensive and non-invasive. It is a measurement of the heterogeneity of the circulating red blood cells size. RDW was previously associated with ventricular dysfunction[5] and other studies support its better prognosis capacity than natriuretic peptides.[6,7] Although it is not completely clear, RDW may be linked to inflammation and ineffective erythropoiesis (for example in renal disease or iron deficiency).[6] In this study, RDW was shown to be highly correlated with disease severity, independent of age, gender and comorbidities but not with mortality.

These biomarkers are not expensive and are available in most hospitals, however they are not routinely used, with the exception of RDW. The information obtained from this article is important, as it adds more data on the use of biomarkers in HF prognosis. More studies with a larger number of patients (and different HF etiologies) are necessary to demonstrate its validity.

This study is limited as it is a single center study, with a small sample size (n=167) and short follow-up (only in-hospital mortality was assessed). Of note, it only included 41.3% of patients with HF with reduced ejection fraction, and all patients had non-ischemic HF.

There are also many other parameters (biomarkers and others) that have been shown to predict morbidity and mortality in HF. However, more than an economic or availability problem, the real limitation of these parameters is their lack of impact on management decisions.

As the authors duly noted, no biomarker is independent from the most important clinical variables, therefore they should not be used for management modification and their use in HF remains academic. With further research, it is hoped that biomarkers can transition from the bench to the bedside.

The search for an ideal biomarker continues as a long overdue promise. Until then, other established laboratory/echocardiographic data and especially clinical status remain paramount to care.

Conflicts of interest

The authors have no conflicts of interest to declare.

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