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EDITORIAL COMMENT

The stress hyperglycemia ratio as risk marker in acute heart failure patients

O rácio de hiperglicemia de *stress* como marcador de risco nos doentes em insuficiência cardíaca aguda

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It is well known that heart failure (HF) is one of the leading causes of mortality and hospitalization in developed countries, and its prevalence is increasing. In Portugal, according to the EPICA study, the prevalence of chronic HF was 4.4%, increasing with age, rising to 12.6% in those aged 70–79 years and exceeding 16% after the age of 80.[1]

HF is a condition associated with high mortality and morbidity, frequent relapses and hospitalizations, entailing high costs and the need for specialized follow-up in dedicated units.[2–4]

The prevalence of HF in Portugal is expected to increase by 30% in 2035 compared to 2011 and by 33% in 2060, resulting in almost 500 000 affected individuals.[5]

A society with a high prevalence of HF, especially in the elderly, is necessarily one with advanced health care, in the 'delayed degenerative diseases' stage of the epidemiological transition. In general, in order to have HF, the patient must have survived other previous cardiac diseases, with adequate prevention, medication and interventions. The most frequent underlying causes of HF are coronary artery disease and hypertension.

In these circumstances, HF represents the terminal station of several lines: coronary artery disease, hypertension, valvular disease, alcoholic cardiotoxicity and others.

Despite the relative success of health care systems that leads to high prevalences of HF by enabling individuals to arrive at this stage of cardiac disease, and although interventions are improving with new approaches and evidence, to date the problem is far from being solved. The introduction of various medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, aldosterone inhibitors, sacubitril/valsartan and recently sodium/glucose cotransporter 2 antagonists), and devices (cardiac resynchronization devices and implantable cardioverter-defibrillators), have led to significant improvements in prognosis.[6] But, even with the best medication and devices, HF remains an ominous prognosis, worse than that of most tumors.

The aging of the population, as well as survival of acute underlying cardiac disease, means that HF is associated with very high and increasing health costs, mortality and morbidity.

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In these circumstances, it makes sense to assess new therapeutic approaches, as well as new prognostic factors that can alter the approach to the disease or improve its course.[7]

In this issue of the *Journal*, Cunha et al. present a paper reporting their retrospective analysis of the role of the stress hyperglycemia ratio in the prognosis of diabetic acute HF patients.[8] They analyzed the influence of the stress hyperglycemia ratio (defined as the ratio of acute to chronic estimated glycemia) on all-cause mortality, with a follow-up of three months.

In a total population of 599 HF patients, mean age 76 years, three-month mortality was 17% (102 patients). The authors used a multivariate model to analyze the factors that contributed to HF mortality in diabetic patients. They found that, together with known risk factors, a low stress hyperglycemia ratio (in the lowest tertile, $\leq$0.88) was associated with a significant increase in three-month mortality risk (hazard ratio 2.24). There was no association between the stress hyperglycemia ratio and mortality in non-diabetic HF patients.

The results are somewhat surprising, because patients with worse prognosis presented a lower acute than chronic glycemic level in acute HF stress. With more severe HF decompensation, increased catecholamine and cortisol release would be expected to lead to a higher acute glycemic level.

The authors explained these results by suggesting that relative hypoglycemia may play a role in short-term mortality in severely ill HF patients. They also point out that an alternative explanation could be diabetic cardiovascular dysautonomia, which would be associated with more severe diabetic disease, leading to a weaker response to stress, and a lower stress hyperglycemia ratio associated with higher mortality.

Another possible explanation could be the general exhaustion of all control systems in advanced HF patients, independent of dysautonomia. The exhausted system is not able to respond to new challenging situations, including HF decompensation. In this context, it is known that overweight is not a risk factor, and is probably protective, in advanced HF patients.

Despite the study's acknowledged limitations (its retrospective nature, small sample size, a single point of acute glycemia measurement, a short three-month follow-up and exclusion of patients who died in-hospital in a condition with high in-hospital mortality), from my standpoint, these results have clinical implications and should be taken into account.

First, acute HF patients should be carefully assessed and, if they are presenting decompensation, routine medication should be revised, particularly diabetic medications, to prevent overtreatment that could result in hypoglycemia episodes.

Second, the stress hyperglycemia ratio could become a new prognostic marker in HF patients. For this, it needs to be confirmed as a risk marker (or risk factor, if it is shown to be reversible) in other studies, ideally prospective.

Finally, with the present high prevalence of HF and its associated morbidity and mortality, I strongly believe that we will need further studies and other approaches to this condition, to continue improving follow-up and prognosis in this common and severe disease.

Conflicts of interest

The author has no conflicts of interest to declare.

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