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Editorial comment

Heart failure after myocardial infarction: Is it all in the risk factors?

Insuficiencia cardiaca tras infarto de miocardio: ¿todo depende de los factores de riesgo?

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In the current era, acute myocardial infarction (AMI) still represents the major cause of de novo heart failure (HF) and it is associated with significant mortality and morbidity, especially in patients with reduced left ventricular ejection fraction (LVEF).[1] Although mortality rates have declined thanks to the advances in the management of AMI, the greater survival and the reduced extent of ventricular injury have led to an increased proportion of older patients with preserved LVEF who remain at high risk of developing HF.[2]

In the study recently published by *REC: CardioClinics*, Melendo-Viu et al. analyzed the incidence, predictors and prognosis of de novo HF in a contemporary cohort of patients with preserved LVEF after AMI.[3] The authors found that 2.8% of these patients were hospitalized for HF during a mean follow-up of 20 months and that age, atrial fibrillation, hypertension and renal dysfunction were independent predictors of post-AMI HF.[3]

The study is consistent with previous reports on the incidence and risk factors for heart failure in the general population. There is a clear relationship between age and HF, which accounts for its increased crude incidence over the last decades, paired with higher life expectancy.[4] Comorbidities are also increasingly common: atrial fibrillation is present in up to 45% of HF patients, hypertension in 76% and chronic kidney disease in 36%. Diabetes mellitus has also been related to the development of HF, although this association was not found in the present study. On the other side, coronary artery disease is indeed a classical risk factor for HF[5]: epidemiological studies have reported a prevalence between 21% and 76% (median 41%) in HF patients.

It is already known that patients who experience myocardial infarction, especially those with reduced LVEF, are at high risk for subsequent HF with a long-term incidence between 4 and 28%.[6] Data from the Valsartan in Acute Myocardial Infarction Trial (VALIANT) trial showed that 10.3% of stable post-myocardial infarction patients with LVEF < 35% developed HF at long-term follow-up, but this proportion reached almost 20% in patients older than 70 years.[7] Another study demonstrated that post- myocardial infarction patients older than 60 years, with left ventricular dysfunction, diabetes and hypertension could have a 5-year risk of HF of 18.8%.[8]

The novelty in the study by Melendo-Viu et al. was the assessment of patients with LVEF > 50% exclusively. In fact, the authors found that the post-MI HF rate in the general cohort was low, as expected in a population with preserved ejection fraction and no previous history of HF, but the combination of age, atrial fibrillation, hypertension and renal dysfunction was associated with almost 20 HF hospitalizations per 100 patient-year, a rate similar to that of patients with left ventricular dysfunction. Therefore, the study remarkably underscores how even patients with preserved LVEF after AMI can be at high risk and that simple clinical risk factors can be as important as more sophisticated measurements, such as left ventricular function, in predicting patient prognosis. Unfortunately, the authors did not provide detailed information on the main diseased vessel, the follow-up of patients not undergoing coronary angiogram, myocardial infarction

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size or troponin levels during the initial episode. De novo HF was defined as any hospital admission by HF after coronary syndrome hospital discharge, but no natriuretic peptides or echocardiographic parameters at the time of HF admittance were reported, which may have led to an underdiagnosis of HF in ambulatory patients and misdiagnosis in some of the admitted patients.

Not surprisingly, the development of HF was associated with a 3–fold increase in mortality in the current study. Mortality remained relatively low overall, with a 10% 1-year mortality in HF patients, compared to 20–29% 1-year mortality in previous studies on HF population.[5] Although causes of death are not specifically described in the current paper, it would be reasonable to think that HF is the driving phenomena and therefore it plays a major prognostic role.

Hence, the aforementioned findings raise a key question for the future: how can we optimally manage these patients in our clinical practice in order to prevent the development of HF after AMI?

Angiotensin-converting enzyme inhibitors, beta-blockers and mineralcorticosteroid receptor antagonists have been shown to improve mortality and decrease HF hospitalizations both in patients with overt HF and reduced ejection fraction and patients with reduced ejection fraction but no signs of HF. Therefore the international guidelines recommend intensive treatment of patients with AMI and LVEF $\leq$ 35%.[9]

Nevertheless, randomized controlled trials have so far failed to show any benefit of the renin-angiotensin system inhibitors in HFpEF patients.[9] Even in the present study, treatment at discharge with beta-blockers or angiotensin inhibitors did not show any potential preventive effect in this population. However, the recently published PARAGON-HF trial (in which almost 40% of patients had an ischemic cause of HF), although missing its primary endpoint of reducing HF hospitalizations and cardiovascular mortality, showed that sacubitril/valsartan might improve outcomes in women and patients with LVEF < 57% and it was associated with a significantly lower rate of worsening of renal function compared to valsartan alone.[10] Thus, in order to prevent the development of HF in post-AMI patients with preserved ejection fraction physicians may need to focus in controlling modifiable risk factors, especially those identified by the authors. Of notice, HF diagnosis was made quite early after hospital discharge for MI: a median time of 5.6 months. Therefore, targeted intervention immediately post-discharge should be considered in high risk patients. For example, avoiding further cardiac ischemic events, which could be responsible for the development of HF, is of utmost importance. In fact, although the authors did not analyze the etiology of post-AMI HF, it is already known that almost one fourth of patients who develop HF after discharge have a recurrent MI, increasing the risk fivefold.[7] Given that ticagrelor has been shown to reduce significantly cardiovascular events and mortality over clopidogrel in post-AMI patients, the use of this drug could be implemented (only 23% of patients were on ticagrelor in the present study), especially in those patients with multivessel disease, which is a strong predictor of post-AMI HF.[11]

Another limitation of the study by Melendo-Viu et al. is that predischarge brain natriuretic peptide (BNP) levels were not reported. Although it has been shown that BNP guided therapy is not effective in preventing HF,[12] the BNP value assessed before discharge could help to diagnose HFpEF during the hospital admission and to stratify post-myocardial infarction patients in order to plan an earlier post-discharge follow-up. In fact, current American Heart Association/American College of Cardiology 2017 HF guidelines[13] recommend the use of natriuretic peptides as a screening tool in patients at risk of developing HF, as it could be useful to prevent the development of left ventricular dysfunction. This recommendation is mainly based on the STOP-HF trial,[14] in which patients with stage A HF (with HF risk factors but no ventricular dysfunction or symptoms) were randomized to standard follow-up or natriuretic peptide screening. Patients with increased natriuretic peptide were further studied with echocardiography and referred to a cardiologist. The study showed a significant reduction in the proportion of left ventricular dysfunction during follow-up.

Overall, the present study shows a low incidence of post-myocardial infarction HF in a big cohort of patients with normal ejection fraction in the new era of treatment. Nevertheless, the minority of patients who develop HF can be identified by simple clinical characteristics that should help us target the subgroup at risk. HF presented early after the initial ischemic episode and was associated with a significant increase in mortality. As cardiologists, our main concern after reading this article should be how to prevent the development of HF in patients with myocardial infarction and to treat comorbidities that make them highly vulnerable. Close follow-up in the first 6 months after myocardial infarction, optimal residual ischemia treatment, natriuretic peptide monitoring and strict control of cardiovascular risk factors, probably through cardiac rehabilitation programs, might be the key to prevention of new-onset HF after ischemic injury.

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