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EDITORIAL

Clinical characteristics and risk factors for mortality on admission in patients with heart failure hospitalized due to COVID-19 in Spain*

Características clínicas y factores de riesgo de mortalidad al ingreso en pacientes con insuficiencia cardíaca hospitalizados por COVID-19 en España

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the SARS-CoV-2 coronavirus that has a high morbidity and mortality. Individuals with chronic diseases, including cardiovascular disease, are more vulnerable.[1,2]

Previous publications indicate that patients with prior heart failure (HF) are a subgroup at greater risk for adverse events in the short- and medium-term.[3,4] In addition, patients infected with COVID-19 have a greater risk of developing acute HF during hospitalization, which entails a worse prognosis.[5]

At present, there is evidence on the physiopathological link between COVID-19 infection and onset of HF.[6] Of note is the tropism of SARS-CoV-2 for vascular cells, with a consequent greater risk of thromboembolic events,[7] and its capacity for infecting cardiomyocytes, as has been demonstrated in confirmed cases of myocarditis.[8]

The article by Salinas-Botrán et al.[9] evaluated the clinical characteristics of patients with a medical history of HF and/or *de novo* HF who were hospitalized for COVID-19. They aimed to identify risk factors of in-hospital mortality. To do so, they retrospectively analyzed data from a multicenter registry from 150 Spanish hospitals (SEMI-COVID-19 Registry) and selected patients with a medical history of chronic heart failure (CHF) or *de novo* HF with confirmed COVID-19 infection from March 1 to October 1, 2020. A logistic regression analysis was conducted to identify risk factors upon hospitalization associated with mortality. They included 1,718 patients (43.5% women; median age 81.4 years). The overall mortality rate was 47.6% (n = 819). The independent risk factors upon admission for mortality were age, severe dependence, tachycardia, C-reactive protein, lactate dehydrogenase (LDH), and serum creatinine.

The authors concluded that patients with HF hospitalized for COVID-19 have a high in-hospital mortality rate and that there is series of simple clinical and analytical factors that can help identify a profile of patients with a worse prognosis.[9]

The article highlighted a prohibitive hospital mortality rate in this subgroup of the population (around 50%), noting variables known to be associated with prognosis and easy to obtain that are predictive of in-hospital mortality. These mortality figures seem considerably higher than other contemporaneous studies.

For example, out of a cohort of 1,212,153 patients with CHF included in the US Premier Healthcare database, Bhatt et al. analyzed 132,312 patients who were hospitalized for any cause in the period from April 1 to September 30, 2020. Of them, a total of 8,383 patients (6.4%) were hospitalized for COVID-19 and the in-hospital mortality rate was 24.2%.[10]

In another study on a cohort of 6,439 patients hospitalized for COVID-19 which compared in-hospital mortality based on the presence of previous HF (422 patients (6.6%)), it was observed that the risk of mortality among patients with HF was twice as high (40.0% versus 24.9%, odds ratio: 2.02; 95% CI 1.65–2.48; $p < 0.001$).[3]

The diagnosis of acute HF in the context of a patient with COVID-19 entails a challenge for the clinician given that both entities share typical symptoms, such as dyspnea and radiological patterns that occasionally overlap. In addition, the elevation of natriuretic peptides, which are so necessary in the diagnosis of HF, can also increase in situations of acute respiratory distress or pulmonary embolism, which are so common in COVID-19.[11] The evaluation of signs of congestion can help establish the differential diagnosis between both

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diseases, though it should not be the only argument for a diagnosis of HF.

There are very few studies which analyze the prevalence of *de novo* HF in patients with COVID-19; they have determined it is infrequent. In the most important study in this regard, which analyzed a cohort of 6,437 patients hospitalized for COVID-19, only 0.6% were diagnosed with *de novo* HF,[12] a result determined when a patient met at least two out of three of the following criteria: (1) signs and symptoms of congestion, (2) BNP > 100 pg/mL or NT-proBNP >300 pg/mL, and (3) chest x-ray compatible with HF (cardiomegaly and/or congestion) or an echocardiogram with systolic/diastolic dysfunction.

In the study by Salinas-Botrán A et al.,[9] the prevalence of *de novo* HF was close to 4%. The criteria of *de novo* HF in this study were clinical parameters of congestion (dyspnea, edema, and increase in jugular venous pressure) indicated on the medical record. The fact that *de novo* HF was predominantly diagnosed by clinical signs and the lack of confirmation with natriuretic peptides and a conventional echocardiogram could be behind such differences and represent a crucial limitation.

The high frequency of mortality in patients with CHF and COVID-19 and the high rate of *de novo* HF reported in this article may be due to differences in baseline risk characteristics, such as an older mean age (81.4 years vs. 63.5 years in the study by Álvarez-García et al.[3]) and greater comorbidity. On the other hand, these differences may also be due to the diagnostic criteria used.

We are aware of the difficulties in systematically conducting a regulated echocardiogram in all patients with COVID-19 infection who are suspected of having HF. However, we believe that to be able to uncover the relationship between COVID-19 and HF with greater certainty, we need to have objective data on structural and/or functional cardiac alterations in those with compatible symptoms.

This study also lacks a control group to be able to compare data and estimate relative risk. Furthermore, future works are needed that help reveal the physiopathological mechanisms underlying this relationship, the phenotypes of HF with greater risk for COVID-19 infection, and variables that better define a worse prognosis. Lastly, the emergence of new COVID-19 variants makes it necessary to constantly reevaluate the relationship between COVID-19 and HF.

References

1. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46:846–8.
2. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5:811–8.
3. Álvarez-García J, Lee S, Gupta A, Cagliostro M, Joshi AA, Rivas-Lasarte M, et al. Prognostic impact of prior heart failure in patients hospitalized with COVID-19. J Am Coll Cardiol. 2020;76:2334–48.
4. Llàcer P, Manzano L, Fernández C, Moreno MC, Núñez J. Mid-term prognostic implication of hospitalized COVID-19 patients with prior heart failure diagnosis. Eur J Intern Med. 2021;88:136–8.
5. Rey JR, Caro-Codón J, Rosillo SO, Iniesta AM, Castrejón-Castrejón S, Marco-Clement I, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. Eur J Heart Fail. 2020;22:2205–15.
6. Giustino G, Pinney SP, Lala A, Reddy VY, Johnston-Cox HA, Mechanick JI, et al. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia: JACC focus seminar. J Am Coll Cardiol. 2020;76:2011–23.
7. Atri D, Siddiqi HK, Lang JP, Nauffal V, Morrow DA, Bohula EA. COVID-19 for the cardiologist: basic virology, epidemiology, cardiac manifestations, and potential therapeutic strategies. JACC Basic Transl Sci. 2020;5:518–36.
8. Bearse M, Hung YP, Krauson AJ, Bonanno L, Boyraz B, Harris CK, et al. Factors associated with myocardial SARS-CoV-2 infection, myocarditis, and cardiac inflammation in patients with COVID-19. Mod Pathol. 2021;34:1345–57.
9. Salinas-Botrán A, Sanz-Cánovas J, Somariba-Pérez J, Pérez-Belmonte LM, Cobos-Palacios L, Rubio-Rivas M, et al. Clinical characteristics and risk factors for mortality upon admission in patients with heart failure hospitalized due to COVID-19 in Spain. Rev Clin Esp (Barc). 2022;222:255–65.
10. Bhatt AS, Jering KS, Vaduganathan M, Claggett BL, Cunningham JW, Rosenthal N, et al. Clinical outcomes in patients with heart failure hospitalized with COVID-19. JACC Heart Fail. 2021;9:65–73.
11. Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid CM, Adamapoulos S, Albert N, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. J Card Fail. 2021;S1071-9164(21):00050–6.
12. Alvarez-Garcia J, Jaladanki S, Rivas-Lasarte M, Cagliostro M, Gupta A, Joshi A, et al. New heart failure diagnoses among patients hospitalized for COVID-19. J Am Coll Cardiol. 2021;77:2260–2.

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