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Echocardiographic findings in critical patients with COVID-19

Hallazgos ecocardiográficos en pacientes críticos por COVID-19

To the Editor,

In the first cases of coronavirus disease 2019 (COVID-19) described in China, acute myocardial injury was identified as being associated with a worse prognosis.[1] The etiology of this myocardial injury is not entirely clear, but it could be related to the processes of microvascular damage, myocarditis, hypoxemia, cytokine-mediated injury, or even stress cardiomyopathy.[2,3] However, diagnosis of myocardial injury has mostly been based on raised biomarkers in the absence of cardiac imaging. In this study, we describe the echocardiographic findings of 37 consecutive patients admitted to the intensive care unit (ICU) with acute respiratory distress syndrome secondary to COVID-19.

This was a prospective, single-center study of consecutive patients with COVID-19, confirmed on polymerase chain reaction testing, who were admitted to the ICU due to acute respiratory distress syndrome. The patients were divided into 2 groups based on whether their left ventricular ejection fraction (LVEF) was greater or less than 50%. In patients with reduced function, the severity of the reduction was estimated qualitatively as mild (40%-49%) moderate (30%-39%) or severe (< 30%). Values of high-sensitivity troponin T, N-terminal pro-brain natriuretic peptide, C-reactive protein, and ferritin were considered inflammatory biomarkers, and their peak levels were recorded and compared between the 2 groups. Echocardiography was performed with a handheld ultrasound (Vscan, General Electrics), with visual assessment of right and left ventricular function on 2-, 3-, and 4-chamber views, to minimize patient exposure. The presence of regional wall motion abnormalities, whether they had coronary or noncoronary distribution, and the presence of pericardial effusion were also assessed. Continuous variables are described as median [interquartile range] or mean ± standard deviation and were compared using the Mann-Whitney U test or Student t test depending on the normality of the distribution of the data. Categorical variables are described as percentage and were compared using the Fisher or chi-square test. Data collection was approved by the ethics committee of our institution.

Table 1
Baseline characteristics of the 37 patients with COVID-19 admitted to the ICU due to acute respiratory distress syndrome

Variable	Total (n = 37)	LVEF < 50% (n = 6)	LVEF ≥ 50% (n = 31)	*P*
Age, y	67.6 [59.6-70.5]	69.6 [68.3-70.8]	65.8 [57.7-70.5]	.117
Male	34 (91.9)	5 (83.3)	29 (93.6)	.421
Ischemic heart disease	2 (5.4)	0	2 (6.5)	.999
Previous systolic dysfunction	0	0	0	.999
Chronic kidney disease	1 (2.7)	0	1 (3.2)	0.999
Chronic lung disease	8 (21.6)	2 (33.3)	6 (19.4)	0.591
ACE-I	17 (45.9)	3 (50)	14 (45.2)	0.999
PaO_2/FIO_2	107.5 [78-125]	99 [85-109]	110 [78-133]	.4225
Biomarkers				
High-sensitivity troponin T (ng/mL)	31.1 [21-103]	210 [28-326]	30.9 [20-81]	.0698
NT-proBNP (pg/mL)	1.367 [766-4.868]	3.023.5 [1.174-7.714]	1.367 [742-4.868]	.5365
CRP (mg/L)	275.5 [187-370]	263 [186-435]	277 [188-361]	.9831
Ferritin (ng/mL)	1.505.5 [663-3.055.6]	1.676.5 [681-3.223]	1.505.5 [583-2.888]	.8318
Echocardiographic findings				
LVEF (%)	55.9 ± 8.9	40.8 ± 3.8	58.9 ± 6.2	.0001
Regional wall motion abnormalities	3 (8.1)	3 (50)	0	.003
Depressed RV systolic function	3 (8.1)	2 (33.3)	1 (3.2)	.015
RV dilation	3 (8.1)	1 (16.7)	2 (6.5)	.425
Pericardial effusion	4 (10.8)	2 (33.3)	2 (6.45)	.055

ACE-I, angiotensin-converting enzyme inhibitors; CRP, C-reactive protein; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; PaO_2/FIO_2, ratio of arterial oxygen partial pressure to fractional inspired oxygen; RV, right ventricle.
Values are expressed as No. (%), mean ± SD or median [interquartile range].

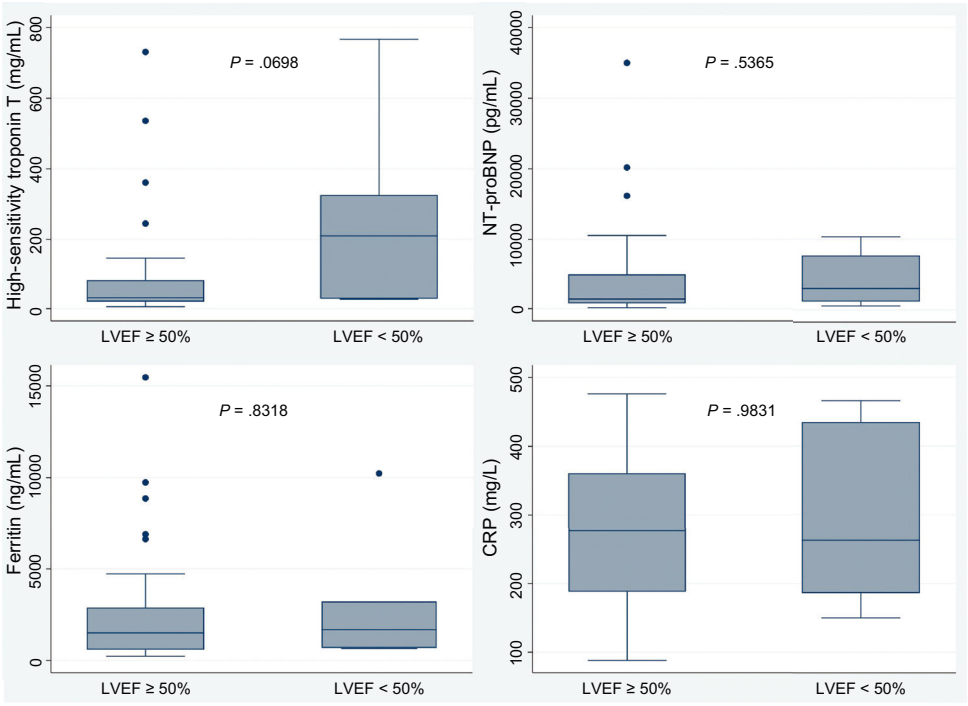

Figure 1. Biomarkers according to the presence of ventricular dysfunction in patients with COVID-19 admitted to the intensive care unit with respiratory distress syndrome. CRP, C-reactive protein; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal brain natriuretic peptide.

During the recruitment period, 38 patients were identified with confirmed COVID-19 and admitted to ICU due to respiratory distress syndrome. In 1 patient, ventricular function could not be assessed due to a poor acoustic window. The median age was 67.6 years and most of the patients were men (91.9%) (table 1). None of the patients had a history of heart failure or known LV systolic dysfunction. The median PaO_2/FiO_2 ratio was 107.5. Six patients (16.2%) had an LVEF < 50% (2 mild, 4 moderate depression). Half of these patients had regional wall motion abnormalities (all with coronary distribution; 2 were inferior and one was anterolateral) and the rest had diffuse hypocontractility. Three patients (8.1%) had reduced right ventricular systolic function (2 of them also had reduced LVEF). There was a high prevalence of pericardial effusion in these patients (33%). The peak high-sensitivity troponin T values were higher in patients with low LVEF (median 210 vs 30.9), although this difference was not statistically significant ($P = .0698$). In contrast, no differences were found in the peak values of N-terminal pro-brain natriuretic peptide, ferritin, or C-reactive protein (figure 1). Of the 37 patients included, 7 (18.9%) died during the median follow-up of 75 [71-82] days, none of whom had reduced ventricular function (mild or moderate depression in all cases). None of the variables analyzed (LVEF < 50%, right ventricular dysfunction, pericardial effusion, or regional wall motion abnormalities) were associated with death or readmission during follow-up. All patients with ventricular dysfunction have been referred for a cardiology appointment in our hospital for further testing once routine tests and procedures can be carried out as normal.

This is the first prospective study in our setting to assess acute myocardial injury in critical patients with severe acute respiratory distress syndrome due to COVID-19 based on biomarkers and echocardiographic findings. The prevalence of reduced LVEF in our series was higher than expected (16.2%) and higher than in previously published retrospective studies. In a recent study of 419 patients with COVID-19, of whom 36 required ICU admission, 11% of this ICU group had LV dysfunction defined as an LVEF < 55%.[4] Deng et al.[5] described a prevalence of LV dysfunction (LVEF < 50%) of 7.5% in a cohort of 67 patients admitted with severe disease. Of note, in our cohort, these patients had higher levels of high-sensitivity troponin T and a higher prevalence of pericardial effusion (33.3%), although this was not associated with increased mortality or readmission, perhaps because the reduction was mild to moderate in all cases.

In our unselected cohort of critical patients with COVID-19 admitted to ICU, LV dysfunction determined on handheld ultrasound was not associated with higher mortality. These results support the recommendations of the Spanish Society of Cardiac Imaging that, given the risk of echocardiography, its use should be limited, even in critical patients, to only certain subgroups of patients such as those with heart failure, arrhythmias, electrocardiographic changes, or cardiomegaly.

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Cardiac magnetic resonance characterization of COVID-19 myocarditis

Caracterización de la miocarditis por COVID-19 mediante resonancia magnética cardiaca

To the Editor,

Since its first description in December 2019 in Wuhan City (Hubei, China), a novel type of mutated coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has infected over 3.6 million people and caused more than 257 000 deaths worldwide (as of May 5, 2020). There is growing concern that acute respiratory disease occurring in coronavirus disease (COVID-19) is strongly associated with cardiovascular damage. Patients with COVID-19 are at risk of cardiac arrhythmias, acute coronary syndromes, heart failure-related events, and fulminant myocarditis.[1] Myocardial injury may occur at different phases of COVID-19 disease (ie, viral, pulmonary, inflammatory, and recovery phase), even late after the onset of symptoms.[2] The mechanisms of cardiovascular injury from SARS-CoV-2 have not yet been fully elucidated and are likely to be multifactorial. SARS-CoV-2 viral particles have been identified by real-time polymerase chain reaction (PCR) testing in cardiac tissue, providing evidence that direct cardiotoxicity might occur.[1] In addition, SARS-CoV-2 has been shown to establish a receptor binding domain with angiotensin-converting enzyme 2 (ACE2) before entering the host cell via endocytosis. Since more than 7.5% of myocardial cells have positive ACE2 expression, this could mediate SARS-CoV-2 entry into cardiomyocytes and cause direct cardiotoxicity.[3] Furthermore, hyperinflammation due to cytokine release mediated by the virus may lead to myocardial and vascular inflammation, plaque instability, a hypercoagulable state, and endothelial cell dysfunction. Finally, cardiac injury may also be mediated by other systemic consequences of COVID-19 infection, including sepsis and disseminated intravascular coagulation. According to postmortem biopsies, the pathological features in cardiac tissue range from minimal changes to interstitial inflammatory infiltration and myocyte necrosis.[1]

We describe 2 different presentations of myocarditis. The first patient was an asymptomatic 26-year-old-pregnant woman diagnosed with gestational diabetes who was admitted for delivery. She required a cesarean section. As part of the preoperative protocol a PCR test was performed, which was positive. The procedure was uneventful and the patient gave birth to a healthy neonate. No abnormalities were observed on a chest X-ray performed the day after surgery and the patient was discharged after 2 days of hospitalization. A week later, she was seen in the emergency department for chest pain radiating to her left arm and was prescribed nonsteroidal anti-inflammatory drugs and colchicine. Due to persistent symptoms and tachycardia, she was admitted to hospital 1 week later. She had no fever or respiratory symptoms. The results of chest X-ray and an electrocardiogram were normal. Echocardiography showed normal systolic function. Troponin T levels were high (319.4 ng/L). The patient underwent cardiac magnetic resonance (CMR) on a 3T system (Magnetom VIDA, Siemens Healthineers, Erlangen, Germany). A conventional CMR protocol to rule out myocarditis was performed. Cine images revealed normal systolic function (left ventricular ejection fraction 59%), with no regional wall motion abnormalities. High signal intensity on T_2 maps (53 ms, normal value $<$ 48 ms) and prolonged native T_1 values were observed in basal and mid-inferoseptal and inferior myocardial segments (1303 ms, normal value $<$ 1200 ms).[4] Late gadolinium enhanced (LGE) images showed mesocardial and subepicardial enhancement of those segments, representing 14.2% of the total ventricular mass (figure 1). Based on CMR findings and the clinical and epidemiological context, a diagnosis of myocarditis due to SARS-CoV-2 infection was established. No myocardial biopsy was performed.

The second patient was a 13-year-old boy who was admitted after 2 days of fever (40 °C). He reported mild cough, odynophagia, abdominal pain, and vomiting in the past few days. Laboratory tests showed mild elevation of C-reactive protein, D-dimer, ferritin, brain

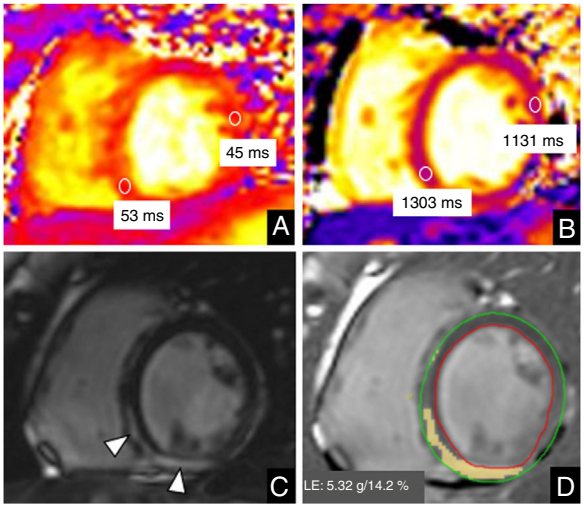

Figure 1. Cardiac magnetic resonance imaging in a 26-year-old woman with COVID-19 myocarditis. Mid-ventricular short axis view. A: T_2 map. B: native T_1 map. C: late gadolinium enhancement (LGE). D: quantification of late gadolinium enhancement. The study revealed slightly increased values on T_2 maps (53 ms vs 45 ms of remote myocardium) and prolonged native T_1 values (1303 ms vs 1131 ms of remote myocardium) in basal and mid-inferoseptal and inferior myocardial segments. These segments showed mesocardial and subepicardial enhancement on LGE sequences (arrowhead in C). The extent of LGE corresponded to 14.2% of the total ventricular mass.