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## Letter to the Editor

### Fulminant myocarditis and cardiogenic shock during SARS-CoV-2 infection<sup>☆</sup>



#### Miocarditis fulminante y shock cardiogénico en el curso de infección por SARS-CoV-2

To the Editor:

Myocarditis is defined as an inflammatory disease of the myocardium, diagnosed using the Dallas criteria, which include histological, (inflammatory infiltrate associated with degeneration and necrosis), immunological and immunohistochemical parameters.<sup>1</sup>

The incidence of myocarditis is difficult to establish since its precise diagnosis relies on endomyocardial biopsies. In general terms, myocarditis is considered to affect 22/100,000 inhabitants.<sup>1</sup>

Regarding its aetiology, there are many factors associated with the development of this pathology and these differ according to geographical location. The viral aetiology is found to be the most frequent cause in developed countries. Other causes such as toxic agents or autoimmune diseases are also frequently responsible for this clinical entity.<sup>1</sup>

The clinical presentation includes numerous signs and symptoms (chest pain, heart failure, ventricular arrhythmias or dyspnoea), with most being nonspecific. A flu-like process is frequently present in the preceding days or weeks in most patients.

Different complementary tests are necessary for its diagnosis. Endomyocardial biopsy is the *gold standard*. The recommended imaging test is a transthoracic echocardiography. Cardiac magnetic resonance imaging may be helpful in identifying the course of myocarditis.<sup>1–3</sup>

There is no specific treatment. Hemodynamic and respiratory support treatment is recommended. The use of anti-inflammatory agents is a controversial issue and antiretroviral therapy is not recommended.

50% of cases will experience full recovery while, on the contrary, with 25% it will lead to severe dysfunction.<sup>1,2</sup>

In December 2019, the first cases appeared of an infection caused by SARS-CoV-2, a type of coronavirus that principally causes a respiratory disease. Cardiac involvement and the development of myocarditis were not frequent.<sup>4,5</sup>

We present the case of a previously healthy, 53-year-old man, who came to the emergency department presenting dyspnoea and 38 °C fever for the past 10 days. He had been in contact with family members infected with SARS-CoV-2. The physical examination showed tachypnoea and work of breathing (WOB). Blood pressure: 94/59, 92% SatO<sub>2</sub>. Cardiopulmonary auscultation was

normal. Blood tests showed a high-sensitivity troponin T level of 555.1 ng/L, leucocytes  $7.6 \times 10^3/\text{mm}^3$  (neutrophils 82.7%, lymphocytes 6.6%). Normal chest x-ray. ECG: sinus rhythm at 133 bpm with diffuse ST-segment elevation. A transthoracic echocardiogram showed a slightly dilated LV with global moderate-severe dysfunction (LVEF 35%). No valvular disease. Normal right cavities.

He was admitted to the intensive care unit with cardiomyopathy of probable viral origin. Cardiotrope virus serologies and blood and urine cultures were obtained - which all gave negative results - and the COVID-19 nasopharyngeal smear was positive.

Treatment was started with a 5.4 µg/kg/min dobutamine infusion. Orotracheal intubation was required due to respiratory compromise. The patient presented progressive hemodynamic deterioration, with clear hypotension, so norepinephrine treatment was started, as well as *de novo* atrial fibrillation which was treated with amiodarone and electrical cardioversion, which were ineffective.

In the following hours, he presented greater hemodynamic instability and increased cardiac enzymes. When a new transthoracic echocardiogram was compared to the previous one, it revealed a decline with LVEF < 10%. Anuria existed despite high doses of furosemide.

Given the poor evolution, a multidisciplinary team discussed the possibility of either implanting a cardiac assist device or the evaluation of placing the patient on the heart transplant list (grade 0 emergency). Finally, the patient died a few hours later in a situation of multi-organ failure.

The clinical presentation of acute myocarditis involves a wide spectrum of symptoms, from chest pain to cardiogenic shock.<sup>1,2</sup>

Coronavirus-19 infection is a global challenge. The mortality of patients with previous cardiovascular disease has increased as a consequence of this infection.

In this case, the patient met the criteria for suspecting fulminant myocarditis: myocardial injury with elevated cardiac enzymes and ventricular dysfunction. The lack of respiratory symptoms despite the COVID-19 infection is an eye-opener, as this is usually the guiding symptom. It is possible that myocarditis has been under-diagnosed in these patients, as the symptoms coincide with cardiovascular alterations (QT lengthening and arrhythmias) described as secondary effects of the administered treatments.<sup>5</sup>

#### Thank you

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<sup>☆</sup> Please cite this article as: Lozano Gómez H, Pascual Bielsa A, Arche Banzo MJ. Miocarditis fulminante y shock cardiogénico en el curso de infección por SARS-CoV-2. *Med Clin (Barc)*. 2020;155:463–464.

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### Strengths and weaknesses of the diagnostic tests for SARS-CoV-2 infection<sup>☆</sup>



### Virtudes y dificultades en los test diagnósticos de la infección por el SARS-CoV-2

To the Editor:

SARS-CoV-2 is an RNA virus belonging to the coronavirus family that causes COVID-19. Since the description in china of the first cases until our current pandemic, this disease has presented major clinical challenges for health systems in every country. From a clinical point of view, it can manifest itself in various ways: from asymptomatic, through bilateral pneumonia, and on to adult respiratory distress syndromes.<sup>1</sup> To date, the diagnosis has been based primarily on tests that confirm the presence of SARS-CoV-2, since the symptoms that patients present can be common to other viruses, bacteria or even some atypical bacteria. We must not forget to evaluate these symptoms so as to rule them out as possible causative agents of the disease we observe. Up to now, when it is suspected that SARS-CoV-2 is the cause of the infection, the *gold standard* determination is *real-time reverse-transcription polymerase chain reaction* [RT-PCR].<sup>2</sup> However, despite the usual high sensitivity and specificity of the RT-PCR tests, on several occasions clinicians have encountered patients with high clinical suspicion (epidemiological, clinical, analytical, and radiological criteria) and with repeatedly negative PCR results. For this reason, first of all we wonder whether the location from where the specimen is obtained is ideal. The test is performed with nasopharyngeal exudate because that is the region where the virus experiences a higher rate of replication. However, other alternative specimens could also be used, such as oropharyngeal exudate, sputum, saliva or bronchoalveolar lavage (the latter implies a greater risk for the personnel who obtain the specimen). Secondly, we question whether the specimen is collected and transported to the laboratory in a suitable manner and without contamination and, thirdly, if the specimen has been optimally processed to obtain the maximum performance of the test.

Given that RT-PCR is a test that requires at least 4–6 hours to complete and its costs are high, recent efforts in the diagnosis of COVID-19 have also focused on *enzyme-linked immunosorbent assays* [ELISA]), and on rapid antigen and antibody tests (Table 1). On the one hand, the ELISA test is an immunoenzymatic test that determines the presence of IgM and IgG antibodies, or a combination of IgM + IgA. The cost of this test is low, and it takes about 3.5–4 hours. On the other hand, the rapid test is a lateral flow chro-

<sup>☆</sup> Please cite this article as: Hernández-Pérez JM, Martín-González E, Pino-Yanes M. Virtudes y dificultades en los test diagnósticos de la infección por el SARS-CoV-2. *Med Clin (Barc).* 2020;155:464–465.

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<https://doi.org/10.1016/j.medcle.2020.07.012>

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matographic immunoassay, and it enables results to be obtained easily in 20–60 min, but with low sensitivity.

**Table 1**

Comparison of the principal diagnostic tests against COVID-19.

	RT-PCR	ELISA test	Rapid antibody test
Type of specimen	Nasopharyngeal or oropharyngeal swab	Serum or plasma	Serum or plasma
Objective	Detection of SARS-CoV-2 virus RNA by exponential amplification of complementary DNA detected in real time	Detection of IgM/IgG or IgG RBD (viral protein receptor-binding domain) antibodies by a colorimetric assay	Detection of IgM/IgG antibodies by colour change of the strip in the lateral flow assay
Advantage	<i>Gold-standard</i> diagnostic test: detects the presence of the virus directly with more precise results at disease onset	Low price, robust detection of seroconversion status, can detect IgM/IgG accurately several days after infection onset	Very low price, easy to use (use at both the point of care and at home), fast results (20–60 minutes) and accurate detection of IgM/IgG several days after infection onset
Limitations	It is a laborious and expensive test, which requires numerous reagents and specialised equipment. It can lose sensitivity after five days from symptoms onset, and it is susceptible to specimen collection errors. Runtime 4–6 hours	Low sensitivity in the first days of illness. Requires rigorous cross-reactivity testing with another immune response and needs to be performed in the laboratory with specialised equipment. Runtime 3.5–4 hours	Low sensitivity in the first days of illness. Requires rigorous cross-reactivity testing

It should be noted that the rapid antibody tests and the ELISA tests provide additional information on the patient's immune status compared to the RT-PCR test<sup>3</sup> (Table 1), although it is still unknown if they can indicate a patient's immunity to future reinfections. The weak points of these techniques are low sensitivity (close to 50%) in the first 7 days of the disease (increasing as days go by to 88%), and the results being affected by the patient's immune status.<sup>4</sup> For these reasons, the information provided by these tests is of little use in many cases and of no use at all in some cases, such as in patients with some types of immunodeficiencies. However, the advantages of the rapid tests include the speed in which they provide the results, simplicity of use and price.<sup>2</sup> In addition, the confirmation of suspected cases of COVID-19 through serolog-