

5. The treatments used in patients with COVID-19 are based on reducing viral reproduction and inflammation (such as 4-aminoquinolone antimalarial agents). However, these drugs could cause cardiotoxicity, with systolic dysfunction and prolongation of the QT interval.<sup>6</sup> Therefore, early markers are required to prevent irreversible cardiotoxicity.

In conclusion, the preventative and therapeutic strategies for COVID-19 will improve with markers that identify those patients with greater pathological, genetic or pharmacological susceptibility to infection with SARS-CoV-2 (ACE2 regulation) and that monitor the mechanisms involved in disease progression (cardiac damage, thrombosis, and cardiotoxicity).

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## Living evidence in response to controversies about the use of antimalarials in COVID-19



### Evidencia viva como respuesta a las controversias en el uso de antimaláricos en COVID-19

#### To the Editor,

The health crisis resulting from the SARS-CoV-2 pandemic has created an area of considerable clinical uncertainty. More answers are needed than the scientific knowledge is able to generate at its usual rate. Currently, we find that there are few completed primary studies on COVID-19, and the preliminary data that have been published provide low evidence levels. Faced with this uncertain situation, the most appropriate thing to do is interpret the available evidence with caution and avoid making precipitate decisions that could be more harmful than beneficial.<sup>1</sup>

In cardiology, several controversial subjects have emerged, such as treatment with angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers used in COVID-19<sup>2</sup> as well as the open debate on chloroquine and hydroxychloroquine that, alone or in combination with antibiotics such as azithromycin and antivirals, are being used to treat the disease.

The boom in these antimalarial drugs in the management of COVID-19 originated in a scientific meeting in China, in the middle of February 2020, attended by the country's clinical trial authors, government authorities, and representatives from regulatory agencies. During that meeting it was concluded that chloroquine

had strong activity against COVID-19 and it was recommended to include it in the guidelines for prevention, diagnosis and treatment of pneumonia caused by COVID-19, issued by the National Health Commission of the People's Republic of China.<sup>3</sup>

Another key moment in the propagation of this idea was when on 19 March a nonrandomized French study, which supported the Chinese hypothesis, was made public.<sup>4</sup> This study was widely shared by unconventional media such as WhatsApp, even before it appeared in the scientific databases. Despite the serious methodological limitations of this study, within hours the message had left its mark. Even the president of the USA stated on the 21 of March on his Twitter account that "Hydroxychloroquine & azithromycin, taken together, have a real chance to be one of the biggest game changers in the history of medicine."<sup>5</sup>

In light of this enthusiasm, the cardiovascular effects of these drugs have been reviewed, and it has been found that, although the incidence of cardiac events is low, they may produce adverse effects such as hypotension or tachycardia (mainly with intravenous administration), QT prolongation (greater with concomitant azithromycin treatment), and interactions with amiodarone, digoxin, and beta-blockers. Clinical recommendations are being issued that advise against concomitant use with amiodarone and suggest monitoring digoxin and QT interval in patients taking hydroxychloroquine and azithromycin.<sup>6</sup>

However, the production of scientific literature regarding COVID-19 is increasing at an incredible, dramatic rate and new publications are appearing rapidly. It is therefore essential that clinicians have tools available that ensure good quality scientific

evidence that is updated almost in real time. One such tool is Living Systematic Reviews, in which systematic reviews are conducted leaving open a review window that allows the incorporation of new evidence as it is published and may even result in changes in the recommendations based on emergent data. These are extremely useful and pertinent to the current situation.

There is already a live repository of scientific evidence on the effectiveness of antimalarials against coronavirus infection that currently includes, among many other things, 20 systematic reviews, 4 clinical trials that report results and 115 registered ongoing randomized trials. This facilitates rapid, effective decision-making with the best and most up-to-date data available.<sup>7</sup>

The COVID-19 pandemic has forced us to adapt our health care and has also shown us that scientific information must be available to clinicians when they need it, which requires an immediate capacity to respond. Meeting this challenge is essential not only for the efficacy of treatments but also for their safety. Live evidence is in the running to be one of great assets of evidence-based practice of our time.

### CONFLICTS OF INTEREST

G. Rada and F. Verdugo-Paiva have links with Epistemonikos and the L-LOVE database for systematic reviews. All authors are members of the COVID-19 L-LOVE Working Group.

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### Cardio-onco-hematology patients' management in the context of the current COVID-19 pandemic



#### Tratamiento de pacientes de cardio-onco-hematología durante la pandemia actual de COVID-19

#### To the Editor,

In the context of the current COVID-19 pandemic, the European Association of Cardiovascular Imaging has published recommendations on precautions, indications, prioritization and protection (for parents and health care workers alike) regarding cardiac imaging studies.<sup>1</sup> However, in this context, there are still insufficient studies on the treatment of cardiotoxicity in patients with cancer to provide official guidelines or a consensus statement. However, the Council of Cardio-Oncology of the European Society of Cardiology has just published an expert opinion on the subject.<sup>2</sup> They emphasize that delaying or avoiding any care required due to the COVID-19 pandemic could result in an increased rate of adverse events. Therefore, a careful risk-benefit assessment should be made for each echocardiogram or cardiology consultation arranged, and the recommendations of the European Association of Cardiovascular Imaging should be followed.<sup>1</sup>

During the current pandemic, patient visits to hospital have decreased to a minimum of essential visits only. In our hospital, cardio-onco-hematology assessment of outpatients is performed in a clinic that is dedicated exclusively to this activity and that has its own echocardiography facilities. Before scheduling any in-person hospital appointment for oncology patients for requested cardiological or echocardiographic review, we carry out a telephone consultation. This telephone consultation firstly may be able to replace certain selected in-person visits, and secondly can also determine the patient's priority. In addition, due to the telephone consultation, we can detect patients with symptoms suspicious for COVID-19 before their in-person visit to organize further assessment.

It should be noted that all the cardio-onco-hematology visits have been coordinated with other essential visits to the hospital (oncology or hematology appointments, intravenous treatment, or blood tests) to ensure these are all done in the same morning and minimize the time in hospital. Patients and hospital staff use the personal protective measures recommended by the health authorities (hand washing or alcohol-based hand gel, masks etc.). Inpatient echocardiograms are performed with a different machine, also in line with the recommendations of the European Association of Cardiovascular Imaging<sup>1</sup>.