Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

of patients had values > 116 mg/dL; that is, they would need drug treatment. Looking at a larger database[6] and without taking diabetes or CVR into consideration, a similar percentage of patients would have to be treated.

In light of the possibility of a huge increase in lipid-lowering treatments, I delved more deeply into the recent recommendations (p. 22).[4] The LDL-C value of < 116 in low-risk individuals is based on reference 36, from 2012, by Mihaylova et al.[7] (also an author of the 2019 guidelines[4]). Hence, the current guidelines used an article from 2012 to support recommendations for 2019.

The study by Mihaylova did not propose any LDL-C target goal, much less 116. It was focused on avoidable events in populations with different CVR levels by decreasing LDL-C by 1 mmol (38 mg/dL), which, parenthetically, yielded a nonnegligible number of patients that would have to be treated.[7]

Where did the authors of the current guidelines get this value of 116? Is there a reference for the article from 2012 in the 2016 guidelines by the same authors? Remember, in 2016 the recommendation was not to intervene if the LDL-C concentration was between 155 and 190 mg/dL (p. 13, Table 5).[5] As the article states: "Low-risk people should be given advice to help them maintain this status" (references 61-71). Furthermore, on page 17 the text says: "... the task force accepts that the choice of any given target goal for LDL-C may be open to debate... (references 65 and 66).

As it turns out, reference 66, which contributes to sustaining these 2 statements, is the same as reference 36 in the 2019 guidelines: the study by Mihylova et al.[7]

In summary, the 2019 European guidelines[4] cite a study from 2012[7] to recommend LDL-C target goals for low-risk patients, but in 2016[5] they use the same reference to support very different recommendations.

What does this mean? And if it were really appropriate to attempt a goal of < 116 mg/dL in low-risk patients, which would imply medicating around 70% of the population, could any health system sustain it?

Juan Carlos Aguirre Rodríguez

Centro de Salud Fortuny, Distrito Sanitario Granada, Granada, Spain

E-mail address: jcaguirre30@hotmail.com

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COVID-19 and treatment guided by biochemical and molecular diagnostic tests to reduce myocardial damage and cardiotoxicity

COVID-19 y tratamiento guiado con tests de diagnóstico bioquímicos y moleculares para reducir el daño cardiaco y la cardiotoxicidad

To the Editor,

Because of the lack of scientific evidence on the effect of cardiovascular treatment on the infectivity of SARS-CoV-2 and on COVID-19 disease progression, the mechanisms that increase the risk of cardiac damage and thrombosis in patients with COVID-19, and the cardiotoxicity of antiviral treatment, we must consider the need for diagnostic tests that help health care professionals when making therapeutic decisions. Important aspects to consider are the following 5 points:

1. Hypertension, diabetes, and cardiovascular disease are the most prevalent comorbidities in patients with COVID-19.[1] Although they do not appear to affect the infectivity of the virus,[2] they do increase disease severity. One of the common mechanisms of this effect is via the renin-angiotensin-aldosterone system. Their treatment reduces levels and activity of angiotensin II, as it contributes to inflammation and endothelial dysfunction. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) and the protease TMPRSS2 to enter the host cell. ACE2 converts angiotensin II into an isoform with anti-inflammatory and vasodilator activity. It has not yet been ascertained whether the overexpression of tissue ACE2, in pathological states or induced by treatment, increases infection with SARS-CoV-2 or makes up for its deficiency to reduce cardiac, pulmonary, and renal inflammation and vasoconstriction. It is also necessary to study the regulation of serum ACE2 levels and its role in reducing the affinity of SARS-CoV-2 for tissue ACE2 and, consequently, infection (figure 1).

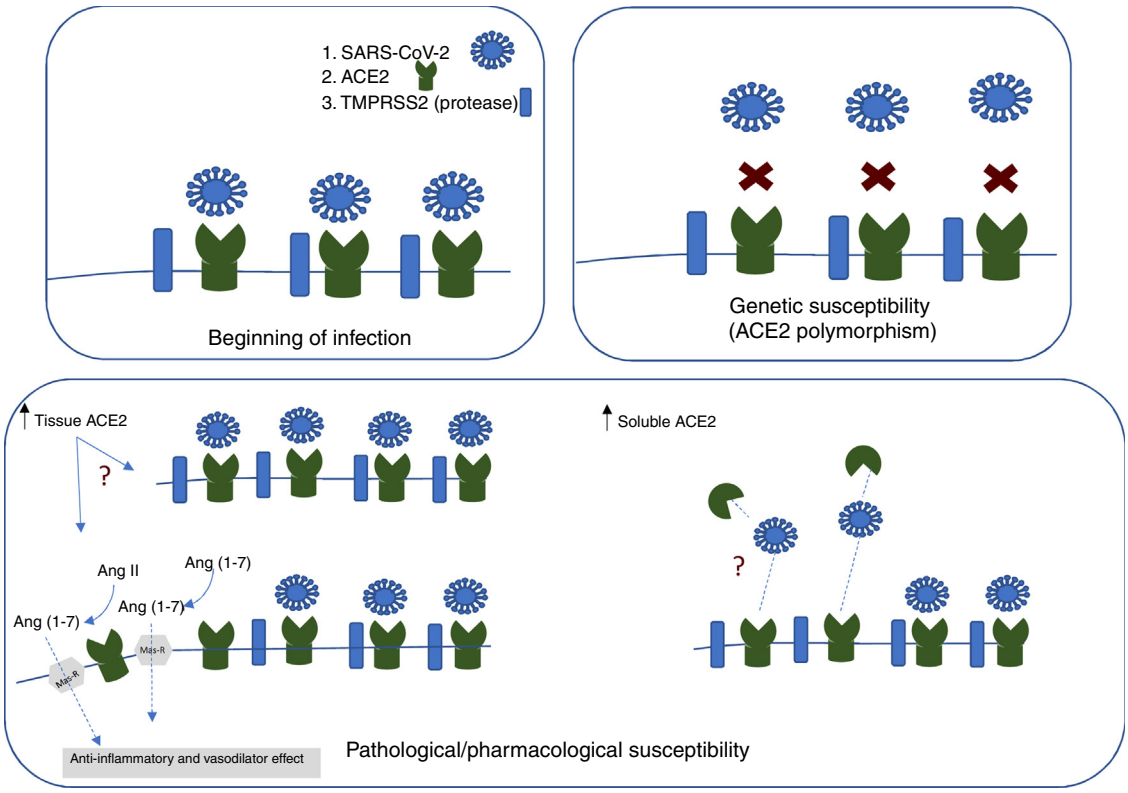

Figure 1. Representation of the importance of angiotensin-converting enzyme 2 (ACE2) and the protease TMPRSS2 for the initial infection with SARS-CoV-2. Polymorphisms of ACE2 or soluble ACE2 may affect its cell binding. The increase in tissue expression of ACE2 may increase the infectivity or have a protective effect, converting angiotensin II to angiotensin (1-7). Ang, angiotensin.

2. Determination of the genetic variants of ACE2 in the population could identify which group has least risk of infection with SARS-CoV-2. Of particular interest would be those described as being associated with essential hypertension (rs2074192) and atrial fibrillation (rs4240157, rs4646155, rs4830542).[3] The variants *SLCO1B1* and *BDKRB2*,[4] associated with patients with toxicity from angiotensin-converting enzyme inhibitors and with symptoms similar to COVID-19, could also be used to exclude false positives.
3. A high percentage of patients with COVID-19 have cardiac events while in hospital. Therefore, there is a strong need for plasma markers of cardiac damage such as high-sensitivity cardiac troponin I or lactate dehydrogenase and markers of cardiac function.
4. There is also a high prevalence of macrovascular and microvascular thrombotic events in patients with COVID-19. High concentrations of D-dimer, a protein degradation product of coagulation, have been shown to be predictors of mortality.[5] However, determination of markers in the initial phase of coagulation could alert to cardiovascular, cerebrovascular, pulmonary, and renal events. We must not forget that ACE2 is expressed in the endothelium and its activation by proinflammatory cytokines triggers the production of tissue factor, platelet adhesion, and activation of the clotting cascade (figure 2).

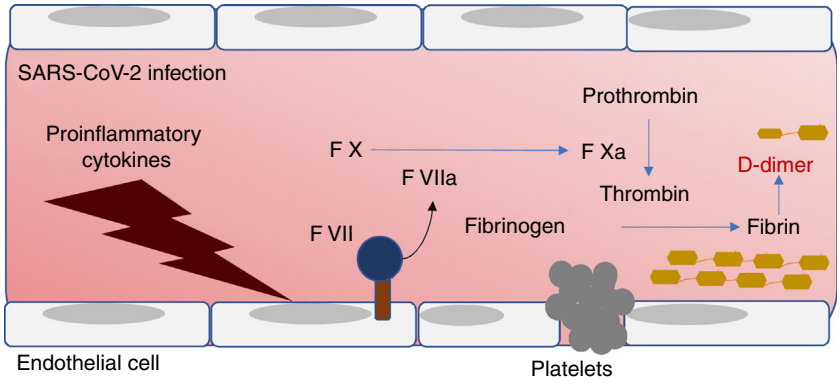

Figure 2. Representation of the coagulation process. Coagulation factors and D-dimer as markers in COVID-19. TF, tissue factor.

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.[6] 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).

Sonia Eiras,[a,b] Ezequiel Álvarez,[b,c] María Brión,[b,d] and José Ramón González-Juanatey[b,c,e,*]

[a]*Grupo de Cardiología Traslacional, Instituto de Investigación Sanitaria, Santiago de Compostela, A Coruña, Spain*
[b]*Centro de Investigación Biomédica en Red Enfermedades Cardiovaculares, CIBERCV, Madrid, Spain*
[c]*Grupo de Cardiología, Instituto de Investigación Sanitaria, Santiago de Compostela, A Coruña, Spain*
[d]*Grupo de Genética Cardiovascular, Instituto de Investigación Sanitaria, Santiago de Compostela, A Coruña, Spain*
[e]*Servicio de Cardiología, Hospital Clínico de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*

[*] Corresponding author:
E-mail address: jose.ramon.gonzalez.juanatey@sergas.es (J.R. González-Juanatey).

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1885-5857/

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.[1]

In cardiology, several controversial subjects have emerged, such as treatment with angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers used in COVID-19[2] 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.[3]

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.[4] 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."[5]

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.[6]

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