

# Les liaisons dangereuses and the danger of deductions: The interplay between cardiovascular disease and COVID-19

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The infection of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), namely coronavirus disease 2019 (COVID-19), has recently become a pandemic, spreading worldwide as rapidly as could not have been thought possible before.<sup>1</sup> The disease has been completely upsetting our society so that every kind of daily behaviour has been adapted and modified; this is evident for scientific and medical communication too. The most important scientific media are answering the need for rapid circulation of information throughout the world, while the external validation of the details is delegated to subsequent analysis and checking. Experimental verification has become empirical in a hypothetical laboratory as big as the entire world.

Moving in this direction, Barison et al. filtered the information that Chinese colleagues had provided through their daily experience and wrote an interesting and pragmatic review.<sup>2</sup> The authors come from Italy and Spain, the two countries in Europe that have been most hit by COVID-19. They have the merit of promoting some reflections for every physician who is professionally involved both in the war against COVID-19 and in treating ‘traditional’ patients without this new disease. The context of the review is very complex and articulated, regarding epidemiology, pathophysiology and therapy of COVID-19. Although the review is very complete, in our opinion some issues are worth further comment.

First, an obvious difference exists between the prevalence of an associated condition in the affected population and its negative prognostic role. In general, we suggest caution in extrapolating the real role of a prognosticator from meta-analyses. They are subjected to adjustments and corrections which are approximate at most, so that estimating the true role of a factor is arduous. As a provoking example, hypertension is prevalent among COVID-19 patients with unfavourable prognosis,<sup>3</sup> but numerically the prevalence is similar to that expected for every age strata in the general population: hypertension is as age-dependent as it is found in COVID-19. Is hypertension really a prognosticator

or only an innocent spectator? There is a compelling need for adjusted analyses, which are solely reliable for guiding preventive and therapeutic strategies. The same can be said for the role of a smoking habit. Asians are less prone to smoke and this could have influenced the statistical models, impairing their validity for Western world inhabitants.

Second, the authors considered, in a comprehensive way, the most frequent drugs administered to patients affected by cardiovascular (CV) disease in the COVID-19 era: this is very timely, appropriate and clinically useful.<sup>2</sup> Regarding renin-angiotensin-aldosterone system (RAAS) inhibitors, the position statement of the European Society of Cardiology<sup>4</sup> is clear and mandatory, but the decision to maintain or to withdraw RAAS inhibitors in critical ill patients is left to an individual physician, with consideration of a number of aspects (e.g. blood pressure, kidney injury, dehydration, heart involvement).

Third, besides the side effects of the anti-COVID-19 therapies (e.g. QT interval prolongation for chloroquine, hydroxychloroquine and azithromycin), Barison et al. highlight the most important aspect not to forget: there are considerable drug–drug interactions between CV therapies and molecules used in caring for COVID-19 patients.<sup>2,5</sup> This is a very relevant issue in everyday clinical practice.

Finally, after two months of difficult cohabitation with SARS-CoV-2 in the Western world, we think that the conclusion of the authors is extremely worthy of sharing:

Patient management should be redefined based on the risk of viral transmission to the medical staff, the

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overlap clinical presentation between COVID-19 and more common acute cardiac diseases, as well as the pharmacological interactions between antiviral, anti-inflammatory and CV drugs.<sup>2</sup>

We consider that cardiologists worldwide should rethink in-hospital management and routine controls of different CV diseases (e.g. heart failure, chronic coronary syndromes) in favour of out-of-hospital diffused and programmed assistance to reduce the risk of infection and guarantee the same level of care to these high-risk patients.

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