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.

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SCIENTIFIC EDITORIAL

The potential sudden shift in clinical research and epidemiology of cardiovascular diseases, caused by COVID-19

L'évolution de la recherche clinique et épidémiologique dans les maladies cardiovasculaires secondaires à l'infection COVID-19

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Background

Coronavirus disease 2019 (COVID-19) is a viral-induced systemic disease that has become a pandemic, producing a public health crisis of unprecedented magnitude. The first epidemic wave has peaked in several countries, including in France a couple of weeks ago, but the infection continues to spread quickly throughout the world, with more than 2,700,000 confirmed cases at the end of April 2020, when this editorial was written [1]. Also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the disease is caused by a novel single-stranded enveloped ribonucleic acid (RNA) virus. The clinical spectrum of COVID-19 ranges from asymptomatic carriers who can transmit the virus to a fatal pleiotropic syndrome. The disease can progress quickly to acute respiratory distress syndrome, with a high fatality rate, especially in patients with pre-existing cardiovascular disease, in whom mortality rates of 10—15% have been recorded [2]. In addition to the common pulmonary presentation, there are also typical cardiovascular manifestations induced

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease 2019; MI, myocardial infarction; MRI, magnetic resonance imaging.

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by COVID-19 [3]. Beyond COVID-19 itself, the confinement on a planetary scale is having major consequences for the epidemiology and public health management of cardiovascular diseases, as well as for cardiovascular research.

Cardiovascular manifestations of COVID-19

As described previously [4], COVID-19 can cause myocardial inflammation and damage, thought to be associated with downregulation of the angiotensin-converting enzyme 2 (ACE2) system [5]. Direct cardiac damage has been shown to affect between 7% and 17% of patients hospitalized with COVID-19, and 59% of patients whose deaths were related to COVID-19 [6]. Myocardial ischaemia has also been described as a potential mechanism of cardiac injury. Indeed, because ACE2 is expressed in the endothelium, it may induce endothelial shedding and dysfunction, leading to vascular damage, local inflammation and the production of procoagulant factors. These mechanisms may underlie the thrombosis and atheroma plaque rupture observed in patients with COVID-19 [7], similar to the increase in type 1 myocardial infarction (MI) described in association with influenza infection [8]. Moreover, type 2 MI resulting from respiratory failure and the viral-induced cytokine storm further aggravates myocardial ischaemia.

Early reports of fulminant myocarditis, assessed by cardiac magnetic resonance imaging (MRI), suggested that myocardial inflammation might play a role in cardiac injury during the viral infection [9]. Indeed, out of a series of 150 COVID-19 cases, 68 deaths were recorded, with 27 cases of myocarditis, including five cases of fulminant myocarditis [10]. Other authors have described autopsy results from patients with COVID-19 as showing a mononuclear infiltrate in myocardial tissue [11]. Moreover, abnormalities of lipid metabolism and lymphopoenia [3] caused by COVID-19 can theoretically lead to a long-term increased risk of cardiovascular events [12].

Finally, because there is a paucity of data on cardiovascular complications resulting from COVID-19, the European Society of Cardiology has recently updated guidelines for the diagnosis and management of cardiovascular diseases in patients with COVID-19 [13].

Delay in the diagnosis and treatment of non-COVID-19 cardiovascular diseases

As part of the public health crisis caused by the COVID-19 epidemic, population confinement, the oversaturation of hospital services and the intense fear of becoming infected may lead to delays in the diagnosis and treatment of cardiovascular diseases unrelated to COVID-19. Indeed, many investigators have reported a reduction in patients admitted for ST-segment elevation MI associated with the COVID-19 pandemic [14]. In addition, an increase of up to 60 minutes in the delay from diagnosis to reperfusion with primary percutaneous coronary interventions has been reported in regions deeply affected by COVID-19 [15]. For those reasons, the Centers for Medicare and Medicaid Services in the USA have recommended that hospitals should consider postponing elective angioplasty during the outbreak [16]. At the end of confinement, the increased demand for cardiovascular healthcare services caused by the delay in patient management may lead to an imbalance between the needs and capacities of cardiologists, primary care physicians and hospitals. Such deviations from optimal care may lead to increased cardiovascular mortality and morbidity [17].

Modified cardiovascular imaging routines because of COVID-19

Diagnostic cardiovascular imaging services have also been affected by the COVID-19 pandemic, with the need to minimize the risk of transmission for patients and healthcare staff. Cleaning and disinfection protocols between each patient, the need for protective equipment and the reduction in the staff numbers have complicated and lengthened imaging examinations. For that reason, the learned societies have proposed guidelines to prioritize patients at highest risk, for whom cardiovascular imaging is likely to substantially change patient management or be lifesaving [18]. As a result, cardiovascular imaging laboratories have cancelled all non-urgent examinations to focus on urgent COVID-19-related diseases, such as myocarditis or severe MI resulting from delayed management as a consequence of the pandemic. In addition, some practices have evolved to reduce the risk of COVID-19 dissemination, such as the use of coronary computed tomography angiography to exclude an acute coronary syndrome in COVID-19 pneumonia with elevated troponins, to prevent unnecessary passage into the catheterization laboratory. Finally, whereas the use of cardiac MRI has fallen during the epidemic because of the risk of contamination, the use of computed tomography has increased proportionally, particularly to rule out left atrial appendage thrombus in patients referred for supraventricular arrhythmia ablation, in substitution of transoesophageal echocardiography.

Consequences of COVID-19 for cardiovascular disease research

Many ongoing clinical studies conducted to evaluate cardiovascular diseases unrelated to COVID-19 have been temporarily suspended by promoters, while regulatory procedures have been dramatically facilitated for COVID-19-related research. Indeed, the studies that are unrelated to COVID-19 often use hard outcomes, such as cardiovascular mortality or non-fatal MI. For that reason, COVID-19-related cardiovascular events would have confounded the evaluation of these outcomes, potentially biasing the results of ongoing clinical trials worldwide.

Conclusions

COVID-19 has had important consequences for the epidemiology of cardiovascular diseases. While the immediate cardiovascular consequences of the infection can be more clearly defined, we may be only beginning to understand the long-term consequences that this crisis may impose

on cardiovascular health and healthcare systems. Finally, beyond developing a successful exit strategy for the present crisis, cycles of acceleration, suppression and re-emergence of COVID-19 have been predicted, for up to at least 12 months. Prolonged awareness, continuous measurement and the ability to adapt to the potential long-term impact of COVID-19 may define the quality of the responses provided by the cardiovascular healthcare system.

Disclosure of interest

The authors declare that they have no competing interest.

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