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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Editorial

Current data on the cardiovascular effects of COVID-19

In December 2019, a series of patients presented with a pneumonia of unknown origin in Wuhan, China. A novel RNA betacoronavirus was identified as the liable pathogen of a highly spread viral pneumonia and was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1,2] The World Health Organization (WHO) named this new viral infection Coronavirus disease of 2019 (COVID-19), and in the middle of March 2020 announced COVID-19 outbreak a pandemic. According to the daily report of the WHO, so far more than 500 000 patients have been affected worldwide and more than 23 000 deaths have been reported.[3] The major transmission route of the disease is human to human through droplets and close contact.[2] The mean incubation period is 5 days, and the spectrum of clinical manifestation ranges from asymptomatic to fever, cough, myalgia, fatigue and to rapid onset of acute respiratory distress syndrome (ARDS) as well as multiple organ failure.[2,4]

A number of studies have shown that there is an association between age, cardiovascular (CV) disease and COVID-19. In a summary of a report from the Chinese Center for Disease Control and Prevention among 72 314 cases records of COVID-19 [confirmed cases: 44 672 (62%)], a total of 10.5%, 7.3%, 6.3%, 6.0% and 5.6% had a history of CV disease, diabetes, chronic respiratory disease, hypertension or cancer, respectively.[5] The overall case-fatality rate (CFR) was 2.3%, but in the age-group 70 - 79 and >80 years the CFR increased to 8.0% and 14.8%, respectively.[5] Similarly, in a meta-analysis that included 1527 subjects with COVID-19 the prevalence of hypertension, as well as cardiac and cerebrovascular disease was 17.1% and 16.4%, respectively.[6] Therefore, preexisting CV disease may be a risk factor for COVID-19.[5] Moreover, small studies in China have shown that patients with established CV disease may be more prone to severe or fatal infection from SARS-CoV-2,[4,7,8] although a study from Italy suggests similar mortality but increased risk for death in people with comorbidities.[9]

To date, the presentation of arrhythmias and elevated cardiac troponin I (cTnI) were reported but it remains unclear which is the specific effect of COVID-19 on the CV system. In patients with hypoxia, in the setting of severe infection or ARDS due to SARS-CoV-2, elevated cTnI levels have been reported which suggests myocardial injury. A meta-analysis of 4 studies in China, with an overall of 341 patients showed that patients with severe COVID-19 had considerably higher cTnI levels in comparison with those who experienced mild disease (standardized mean difference: 25.6 ng/L; 95% confidence intervals: 6.8-44.5 ng/L).[10] Both ischemic and non-ischemic myocardial conditions such as myocarditis may cause myocardial injury.[11,12] Retrospective studies in hospitalized patients in China, showed that cardiac injury was more common in patients admitted to the intensive care units (ICU) and among those who died; thus it may be correlated with worse prognosis.[7,11,13] A recently published case report showed that a man who was admitted to the hospital in China due to chest pain and dyspnea for three days and presented ST-segment elevation on the electrocardiogram (ECG), increased cardiac biomarkers as well as left ventricular dysfunction in the echocardiogram, had no signs of coronary stenosis in the CT coronary angiography; the coronavirus nucleic acid test was positive.[14] Interestingly the patient was treated with methylprednisolone and intravenous immunoglobulin added on antibiotics, and after three weeks the ventricular function as well as the myocardial injury markers had fully recovered to the normal range.[14] It should be noted that there are limited data regarding the association of acute coronary syndrome and COVID-19.

Another common cardiac manifestation in people with COVID-19 is cardiac arrhythmias. In a cohort study of 137 patients admitted in tertiary hospitals in Hubei, a percentage of 7.3% of them presented heart palpitations as the initial symptom.[15] A previously study found also that cardiac arrhythmias were almost double in ICU patients in comparison with non-ICU patients [16 (44.4%) Vs 7 (6.9%), $p < 0.001$].[7] The specific type and the underlying mechanisms of reported arrhythmias have not yet been elucidated. An underlying myocarditis, could be a reasonable explanation in COVID-19 patients experiencing cardiac injury, in terms of elevated cTnI with new onset arrhythmia. A study showed that the prevalence of heart failure was 23% among patients with COVID-19.[11] However, it remains unclear whether new cardiomyopathy (i.e. due to myocarditis) or worsening of an underlying myocardial dysfunction could explain the high prevalence of heart failure in this population.[16,17] It should be noted that pericardial involvement has not been reported yet. Data regarding the cardiovascular complications in patients with COVID-19 are presented in Table 1.

To date, the pathophysiology of high pathogenicity of SARS-CoV-2 in elderly people or in people with severe comorbidities has not been totally understood. Previous studies demonstrated that COVID-19 patients had high levels of proinflammatory cytokines such as interleukin (IL) −1, IL-6, interferon gamma (IFN-γ), IFN inducible protein-10 (IP- 10), and monocyte chemoattractant protein-1 (MCP-1), which probably led to the activated T-helper-1 cell response.[13] Additionally, it was reported that patients who required ICU admission had higher concentrations of granulocyte colony stimulating factor (GCSF), IP10, MCP-1, macrophage inflammatory protein -1A (MIP-1A) and tumor necrosis factor - a (TNF-a) compared to non-ICU patients.[18] It is postulated that this cytokine storm may be correlated with disease severity and outcome.[13,18]

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Table 1
Cardiovascular complications in patients with COVID-19

	Study	Patients	Outcomes
Arrhythmia	Wang 2020,[7] retrospective, single-center case series	138 hospitalized patients	Total events: 23 (16.7%) ICU vs non-ICU patients: 16 (44.4%) vs. 7 (6.9%), p < 0.001)
	Liu 2020,[15] retrospective, nine- tertiary hospitals (cohort)	137 hospitalized patients	Total events: 10 (7.3%)*
Myocardial injury (elevated cTnI)	Huang 2020,[13] retrospective, cohort study	41 hospitalized patients	Overall: 5 (12%) ICU patients: 4 (31%) Vs. non-ICU patients: 1 (4%), p = 0.017
	Wang 2020,[7] retrospective, single-center case series	138 hospitalized patients	Overall: 10 (7.2%) ICU patients: 8 (22.2%) Vs. non-ICU patients 2 (2.0%), p < 0.001
	Zhou 2020,[11] retrospective, multicenter cohort study	191 hospitalized patients	Overall: 33 (17%) Survivors: 1 (1%) Vs. non survivors: 32 (59%), p < 0.0001
Myocarditis	Ruan 2020,[20] retrospective, multicenter study	68 deaths from 150 hospitalized patients	5 (7%) deaths from myocardial damage and circulatory failure 22 (33%) deaths from myocardial damage and respiratory failure**
Heart Failure	Zhou 2020,[11] retrospective, multicenter cohort study	191 hospitalized patients	Overall: 44 (23%) Survivors: 16 (12%) Vs. non-survivors 28 (52%), p < 0.0001

Data are presented as n (%).
Abbreviations: cTnI, cardiac Troponin I; ICU, intensive care unit.
* Patients presented heart palpitations as initial symptom.
** Some patients died of myocarditis.

In particular, a study demonstrated that patients who were infected from SARS-CoV-2 and presented myocardial injury had high IL-6 levels, and death was associated with cardiac damage induced by fulminant myocarditis.[16] Moreover, cases of acute myocarditis using cardiac magnetic resonance imaging that were attributed to other coronavirus species such as the middle east respiratory syndrome coronavirus (MERS-CoV) have been reported.[19] An analysis of 150 patients with COVID-19, showed that among 68 fatal cases, 5 people (7%) with myocardial damage died of circulatory failure and 22 (33%) died of both myocardial damage and respiratory failure.[20] At last, reports from heart autopsy in COVID-19 patients with high viral load showed an inflammatory mononuclear infiltrate in myocardial tissue, which also supported the clinical scenario of fulminant myocarditis.[15,21,22]

SARS-CoV-2 invades host cells through the angiotensin converting enzyme 2 (ACE2) protein.[2] Angiotensin-converting-enzyme inhibitors (ACE inhibitors) and angiotensin II receptor blockers (ARBs) drugs are commonly used especially among people with CV disease. There is evidence from animal studies that mainly ARBs and maybe ACE inhibitors, upregulate membrane-bound ACE2.[23] However, the upregulation is observed after high dose administration of ARBs in animals and not in doses commonly used in humans; in addition, the upregulation has been documented mainly in cardiac and renal tissue and not in the lungs.[23] Experimental data have shown that transgenic mice that overexpress ACE2 are prone to extensive lung injury after infection with SARS-CoV.[24] On the other hand, transgenic mice deficient for ACE2 showed severe acute lung failure during sepsis or infection with viral agents including SARS-CoV[25]; moreover, treatment of the mice with recombinant ACE2 prevented acute severe lung injury.[25] Another point that should be addressed is the following: during acute lung injury, alveolar ACE2 appears to be downregulated.[23] This would decrease angiotensin II metabolism, resulting in higher local levels of this peptide, which increases alveolar permeability and accelerates lung injury.[23] Given this fact, one can speculate that having increased ACE2 expression by preexisting ARBs treatment may actually be protective for the lungs in the course of SARS-CoV-2 infection. Therefore, the data so far in humans indicate that there is no evidence for a potential beneficial or harmful effect of ACE inhibitors or ARBs during infection with the SARS-CoV-2.

The extend and severity of myocardial injury in patients affected by SARS-CoV-2 is not known since data from histological, imaging, and other studies are limited. From the clinical point of view the data so far indicate that myocardial injury may occur in patients with severe infections from SARS-CoV-2 who need hospitalization and/or ICU support. Respiratory failure and severe myocardial injury and/or arrhythmias are the most known causes of death in critically ill patients. However, palpitations as a symptom was reported by 7.3% of the affected from SARS-CoV-2 patients early in course of the disease and may be indicative of myocardial involvement[15]; in such patients monitoring of myocardial enzymes and/or ECG for life-threating arrhythmias may be warranted.

In conclusion, COVID-19 has been associated with multiple direct and indirect CV complications including acute myocardial injury, myocarditis as well as arrhythmias and the CV community will play a major role in the management of people affected by this disease.

Conflict of interest

There is no conflict of interest.

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