

Focus on COVID-19

Impact on the cardiovascular system

Introduction

The global spread of coronavirus disease 2019 (COVID-19) persists. With over 3 million infections and more than 210,000 deaths to date, the pandemic continues to present significant challenges to health systems around the world, and across all branches of medicine.

In response to the COVID-19 pandemic, the scientific community has united to tackle the disease, with many studies initiated to understand its mechanism and treatment options. Scientific societies have provided guidance for the treatment of patients with comorbidities, and journals have provided open access to scientific literature in an attempt to disseminate knowledge and contribute to better outcomes.

Here, we focus on the implications of the COVID-19 pandemic for *cardiovascular medicine*. Emerging studies address how COVID-19 impacts the cardiovascular system, the status of prospective treatment approaches, and the importance of safety for healthcare providers on the frontline.

The information included acknowledges the significant contribution of researchers, scientific societies and publishers, and does not necessarily reflect a position of Edwards Lifesciences in relation to individual studies.

Section 1: COVID-19 and the cardiovascular system

A growing body of evidence now links COVID-19 with cardiovascular complications. Myocardial injury is evident in over a quarter of critical patients with COVID-19, presenting either as acute myocardial injury, or developing as the illness intensifies.

Data suggest that the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) virus invades cardiomyocytes by binding to angiotensin-converting enzyme 2 on the cell surface, resulting in myocardial injury which elevates troponin I levels. Studies of patients with COVID-19 in China indicate a significantly higher in-hospital mortality rate in patients who also have myocardial injury.

Acute infections increase the risk of acute coronary syndrome. COVID-19 may increase circulating cytokines, which have the potential to cause instability and rupture of atherosclerotic plaques.

Fever, stress, electrolyte disturbances and use of antiviral drugs in patients with COVID-19 may all have pro-arrhythmic effects. This may be an issue for patients with inherited arrhythmia syndromes, such as long QT syndrome, Brugada syndrome, short QT syndrome and catecholaminergic polymorphic

ventricular tachycardia. For these patients, additional precautions and specialised management are advised.

A series of four autopsies carried out in New Orleans following COVID-19-related deaths recorded diffuse alveolar damage, a microembolism potentially associated with sepsis, and significant haemorrhage. In each heart, scattered individual cell myocyte necrosis was noted indicating damage. A significant lack of myocarditis was observed; the rise in brain natriuretic peptide seen in at least one case was likely to result from acute ventricular dilatation. The underlying cause of myocyte degeneration remains unclear.

Finally, COVID-19 might have several implications for cardiac patients with pre-existing associated comorbidities such as chronic renal disease, diabetes or in those requiring heart transplantation. In addition to the risks of exposure to the virus in hospital, COVID-19 may impact donor selection, immunosuppression, and post-transplant management.

The publications detailed below may prove useful in understanding the impact of COVID-19 on the cardiovascular system.



Coronavirus Disease 2019 (COVID-19) and cardiovascular disease

Clerkin KJ et al. *Circulation*. 2020; Mar 21.

 <https://bit.ly/2Y3vs5Z>

Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts

Nicin N et al. *Eur Heart J*. 2020; April 15.

 <https://bit.ly/3bzWzP5>

Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality

Bonow RO et al. *JAMA Cardiol*. 2020; March 27: e1–3.

 <https://bit.ly/2xKhhYr>

SARS-CoV-2, COVID-19 and inherited arrhythmia syndromes

Wu CI et al. *Heart Rhythm*. 2020; March 31.

 <https://bit.ly/351gwad>

Pulmonary and cardiac pathology in Covid-19: The first autopsy series from New Orleans

Fox SE et al. *medRxiv*. 2020; April 10.

 <https://bit.ly/3ax4c2E>

Section 2: Treatment evidence update

A growing number of studies have reported on potential treatments for COVID-19, including antiviral and antimalarial therapies. Published studies range from small case reports to larger randomised controlled trials. Many studies are ongoing as the response to the pandemic intensifies globally.

One of the few randomised controlled trials to be published to date found no benefit above the standard of care for the combined antiviral treatments lopinavir and ritonavir. This was in hospitalised adult patients with severe COVID-19, despite their previous efficacy against the 2003 SARS CoV virus. Remdesivir, a broad-spectrum investigational antiviral drug, which targets RNA replication, is undergoing trials for COVID-19 following support from the World Health Organization. Remdesivir targets RNA replication, required for SARS-CoV-2 infection, and has shown promising results *in vitro* and in preclinical studies. Chloroquine, an antimalarial drug, and hydroxychloroquine, used in rheumatoid arthritis and systemic lupus erythematosus, have gained widespread publicity in the fight against COVID-19. Although, a study of 181 patients hospitalised for COVID-19 infection and requiring oxygen found no

evidence of efficacy of hydroxychloroquine. Other drugs under investigation include, for example, the antivirals: ribavirin, sofosbuvir, galidesivir and tenofovir, and the antibacterial: teicoplanin. Currently, the treatment landscape remains fluid, recently including transfusion of 'convalescent plasma' and strategies to block interleukin-6 to mitigate the cytokine storm in severely ill patients, including the use of tocilizumab, which has shown promise in initial studies to date. Further studies will be required to gain a picture of the best approaches to manage patients with COVID-19.

The publications below provide insight into potential COVID-19 treatments.

A trial of lopinavir–ritonavir in adults hospitalized with severe COVID-19

Cao B et al. *N Eng J Med*. 2020; March 18.

 <https://bit.ly/2x88MGU>

No evidence of clinical efficacy of hydroxychloroquine in patients hospitalised for COVID-19 infection and requiring oxygen: Results of a study using routinely collected data to emulate a target trial

Mahévas M et al. *medRxiv*. 2020; April 14.

 <https://bit.ly/2KxLxJw>

Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence

Cao YC et al. *Travel Med Infect Dis*. 2020; April 2.

 <https://bit.ly/2KxLHAC>

Ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): A molecular docking study

Elfiky AA. *Life Sci*. 2020; **253**: 117592.

 <https://bit.ly/3bBFIGP>

Teicoplanin: An alternative drug for the treatment of COVID-19?

Baron SA et al. *Int J Antimicrob Agents*. 2020; **55**: 105944.

 <https://bit.ly/3cHMcuE>

Interleukin-6 in COVID-19: A systematic review and meta-analysis

Coombes EA & Haghbayan. *medRxiv*. 2020; 03.30.20048058.

 <https://bit.ly/3eVdn02>

Section 3: Comorbidities

From the outset of the COVID-19 pandemic, an association between specific comorbidities, which are often present in cardiac patients, and poorer outcomes for patients has been apparent. Medical societies and specialists have published position statements providing guidance on how to treat patients with specific comorbidities in the COVID-19 setting (Table 1). As patients with cardiovascular disease often have additional risk factors, for example renal disease and diabetes, treatment of these patients should be aligned with guidance from the relevant medical societies.

Table 1: Guidance for patients with specific comorbidities

Comorbidity	Useful links
Sepsis	https://bit.ly/sepsis_guidance
Respiratory	https://bit.ly/respiratory_guidance
Hypertension	https://bit.ly/hypertension_guidance
Renal disease	https://bit.ly/renal_guidance
Diabetes	https://bit.ly/diabetes_guidance
Liver and gastrointestinal disease	https://bit.ly/liver_guidance
Transplantation	https://bit.ly/transplantation_guidance

Section 4: Hospital staff safety

Hospital staff are on the front line in the fight against COVID-19 and are at high risk of exposure to the virus, especially in the Intensive Care Unit (ICU). Safety of staff is therefore a primary concern in the treatment of patients with COVID-19.

Aerosol-generating procedures, such as intubation can contaminate healthcare workers and the surrounding environment, highlighting the need for appropriate personal protective equipment (PPE). New approaches to protect healthcare workers, including the use of a protective box around patients in the ICU have been proposed, but may not be practical in all situations. Laboratory staff may also be at risk of exposure to the virus, emphasising the

need to follow universal standard precautions during the analysis of samples. Experience from China indicates that adopting and rigorously enforcing adequate precautions can prevent healthcare workers from becoming infected with COVID-19. However, providing constant and adequate supplies of PPE is a major challenge, especially in the context of disrupted supply chains.

The following publications detail some implications of COVID-19 that individuals on the front line face.

Barrier enclosure during endotracheal intubation

Canelli R *et al.* *N Eng J Med.* 2020; April 3.

 <https://bit.ly/3eJlnkK>

The COVID-19 pandemic: Implications for the cytology laboratory

Stefan E. *J Am Soc Cytopathol.* 2020; March 26.

 <https://bit.ly/2XX3M2S>

Death from Covid-19 of 23 health care workers in China

Zhan M *et al.* *N Eng J Med.* 2020; April 15.

 <https://bit.ly/3bG9oTi>

Predicting the impacts of epidemic outbreaks on global supply chains: A simulation-based analysis on the coronavirus outbreak (COVID-19/SARS-CoV-2) case

Ivanov D. *Transport Res Part E: Logist Transport Rev.* 2020; 136: 101922.

 <https://bit.ly/3cH6vI2>

Section 5: Registries of interest in the cardiac field

Clinical registry data provide valuable information on characteristics, treatment, and outcomes of patients hospitalised, including patients with cardiovascular disease.

Several registries and online tools have now been developed or adapted to collect information on treatments and outcomes for patients with COVID-19 (Table 2). Given the strain associated with COVID 19 on healthcare systems, some registries have taken steps to streamline and automate data entry so that the burden of participation is reduced.

Table 2: Registries and online tools for patients with COVID-19

Registry	Focus
American Heart Association: Get With The Guidelines https://bit.ly/GWTG_registry	<ul style="list-style-type: none"> Data on patients with atrial fibrillation, coronary artery disease, heart failure, stroke and in-hospital cardiac arrest COVID-19 specific data elements added
Extracorporeal Life Support Organization https://bit.ly/ELSO_registry	<ul style="list-style-type: none"> Data on outcomes following extracorporeal membrane oxygenation (ECMO) in COVID-19 cases
European Society of Cardiology https://bit.ly/ESC_registry	<ul style="list-style-type: none"> Improve knowledge of the role of cardiovascular disease in COVID-19 Generate standardised and co-ordinated data
Society of Thoracic Surgeons (STS): COVID-19 Resource Prediction Instrument https://bit.ly/STS_registry	<ul style="list-style-type: none"> Developed to assist healthcare providers in triaging adult cardiac surgery cases Provides estimate of ventilator hours, ICU time, transfusions, and risk of acute reoperation

The role of data registries during COVID-19

Real-world registries provide valuable insight into the patient characteristics, treatment and outcomes of patients with COVID-19. This paper provides a list of ongoing registries, which now allow COVID-19 specific data entry.

Alger HM et al. *Circulation: Cardiovasc Qual Outcomes*. 2020; April 16.

 <https://bit.ly/2zs2R08>

Section 6: Useful links

Many societies and journals have provided open access to COVID-19 studies (Table 3) in a welcome gesture to promote scientific knowledge and collaboration, for which they need to be acknowledged.

Abbreviations

- COVID-19: coronavirus disease 2019
- ECMO: extracorporeal membrane oxygenation
- ICU: intensive care unit
- PPE: personal protective equipment
- SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Table 3: Society and journal links to COVID-19 information

Society/Journal	Link to COVID-19 information
American College of Cardiology	https://bit.ly/ACC_advice
Circulation	https://bit.ly/Circ_advice
Clinical trials.gov	https://bit.ly/clintrials_advice
European Association for Cardio-Thoracic Surgery	https://bit.ly/EACTS_advice
European Society of Cardiology	https://bit.ly/ESC_advice
Journal of Thoracic and Cardiovascular Surgery	https://bit.ly/JCTVS_advice
Lancet	https://bit.ly/Lancet_advice
New England Journal of Medicine	https://bit.ly/NEJM_advice
Oxford University Press	https://bit.ly/Oxford_advice
Springer	https://bit.ly/Springer_advice
Society of Thoracic Surgeons	https://bit.ly/STS_advice

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