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# Cardiology and COVID-19: A bidirectional association!

## To the Editor

The novel corona virus pandemic has the world in its grip and infection with COVID-19 has proven to be beyond a pulmonary disease. There are pre-existing cardiac conditions predisposing to it and the cardiological manifestations of the disease are being increasingly recognised.

The previous viral pandemics and epidemics have shown that viral infections are more likely to occur in patients with underlying cardiovascular disease [1]. Viral myocarditis is a prominent infectious-inflammatory disease reported with the previous corona virus epidemics [2, 3]. Even long-term follow up of the survivors of the previous viral epidemics has documented cardiovascular and metabolic abnormalities [4].

The published medical literature on COVID-19 relevant to cardiology is summarised in Table 1. There is mounting evidence that underlying cardiovascular conditions lead to a higher likelihood of infection, more severe disease progression, and a greater risk for mortality from COVID-19. Also, studies evaluating patients with COVID-19 presenting with cardiac injury show that they have a poorer outcome. It is important for physicians to realise the importance of cardiac disease as a risk factor and potential complication of the disease because this might help in improving the management and treatment of infected patients.

Early measurement of cardiac biomarkers (troponin and NT-pro BNP) of a suspected infected patient can help identify cardiac injury. However, it is important to realise that biomarkers of cardiac injury often rise in hospitalized patients and that its interpretation and actionability would require careful consideration. Electrocardiography (ECG) is instrumental in assessing for arrhythmia, and echocardiography (ECHO) is a convenient bedside test to assess for cardiac systolic and diastolic function. The other test for assessing cardiac function is a cardiac MRI. CT and Doppler may assist in detecting the thrombotic complications in a patient.

It is still not clear whether the cardiac manifestations are because the cardiac myocytes are the primary target or secondary bystander. Minimally invasive autopsies from lung, heart, and other sites of COVID-19 patients have shown that, while the virus does have a predilection for the lungs, the infection also results in damage to the heart, vessels, liver, kidney, and other organs [5]. Cardiac manifestations are likely due to a multifactorial aetiology; the myocardial damage could be related to the direct effect of the virus or may occur indirectly with increased oxygen demands due to tachycardia and fever, and reduced oxygen delivery due to hypotension and hypoxemia. Another possibility is that the enhanced inflammatory state can induce vascular inflammation, myocarditis, and cardiac arrhythmias [6]. The resulting cytokine storm can elicit activation of cells within pre-existing atherosclerotic lesions thus augmenting thrombotic risk and risk of ischemic syndromes. Moreover, microvascular activation by cytokines can cause myocardial injury along with harm to other organ systems [7]. Besides these causes, the possible impacts of the drugs currently used to treat COVID-19 cannot be ignored. Some of the drugs that are frequently used to manage these cases are known to prolong the QT interval and can have a proarrhythmic propensity resulting in cardiac complications [8, 9].

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**Table 1. Summary of the medical literature on COVID-19 and cardiology**

| Author, country | Type of article | Number of patients | Cardiology relevant findings | Implications/conclusions |
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| Aghagoli *et al.* [10], all trials are from China | Meta-analysis | Six studies* with 1527 patients | **Pre-existing conditions:**<br>Hypertension — 17 %, cardia-cerebrovascular disease — 16.4%, diabetes — 9.7%<br>**Cardiac complications:**<br>At least 8.0% suffered from acute cardiac injury<br>13 folds higher in ICU/severe patients compared with the non-ICU/severe patients | Patients with previous cardiovascular metabolic diseases may face a greater risk of developing the severe condition |
| Shi *et al*. [11], China | Cohort study | 416 patients | **Cardiac complications:**<br>Cardiac injury — 19.7%<br>Patient with cardiac injury were older and had more co-morbidities | Deaths were more common in patients with cardiac injury than those without |
| Zhou F *et al.* [12], China | Retrospective, multicentre cohort study | 191 patients (137 discharged and 54 died) | **Pre-existing conditions:**<br>Hypertension — 30%, diabetes — 19%, coronary heart disease — 8%<br>Increasing odds of in-hospital death associated with elevated d-dimer on admission. | d-dimer could help clinicians to identify patients with a poor prognosis at an early stage |
| Deng Y *et al.* [13], China | Retrospective study | 225 patients (109 died and 116 recovered) | **Pre-existing conditions:**<br>**A. Hypertension:**<br>Death group — 36.7%, recovered group — 15.5%<br>**B. Diabetes:**<br>Death group — 11.9%, recovered group — 3.4%<br>**C. Cardiac complications:**<br>Acute cardiac injury<br>Death group — 59.6%, recovered group — 0.8%<br>Disseminated intravascular coagulation<br>Death group — 6.4%, recovered group — 0% | More patients in the death groups had complications such as acute cardiac injury, shock, and DIC |
| Chen T *et al.* [14], China | Retrospective case series | 274 cases (113 died and 161 recovered) | **Pre-existing conditions:**<br>**A. Chronic hypertension:**<br>Death group — 48%, recovered group — 24%<br>**B. Other cardiovascular comorbidities:**<br>Death group — 14%, recovered group — 4%<br>Concentrations of creatine kinase, cardiac troponin I, N-terminal pro-brain natriuretic peptide, and D-dimer were markedly higher in deceased patients than in recovered patients<br>**Common cardiac complications:**<br>Acute cardiac injury — 77%, heart failure — 49% | Patients with cardiovascular comorbidities were more likely to develop cardiac complications<br>Regardless of history of cardiovascular disease, acute cardiac injury and heart failure were more common in deceased patients |
| Du Y *et al*. [15], China | Retrospective chart review | 85 fatal cases | **Pre-existing conditions:**<br>Hypertension — 37.6%, diabetes — 22.4%, CAD — 11.8%<br>**Complications:**<br>Respiratory failure — 94.1%, shock — 81.2%, ARDS — 74.1%, arrhythmia — 60.0%, acute myocardial injury — 44.7%, acute liver injury — 35.3%, sepsis — 32.9% | The majority of the patients died of multiple organ failure |

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| Li *et al*. [16], China | Retrospectively enrolled and followed up | 548 patients (269 severe and 279 non-severe) | **Mortality:**<br>1.1% in non-severe patients<br>32.5% in severe cases<br>Elder age, underlying hypertension, high cytokine levels and high LDH level were associated with severe disease<br>**Factors associated with seath:**<br>Cardiac injury, high LDH, hyperglycemia, high-dose corticosteroid | Elderly patients with hypertension and high LDH levels need careful observation and early intervention |
| Klok FA *et al.* [17], Netherlands | Prospective study | 184 ICU patients | CTPA and/or ultrasonography confirmed VTE in 27% and arterial thrombotic events in 3.7% | Recommend strict application of pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to the ICU |
| Richardson S *et al.* [18], USA | Prospective | 5700 patients | **Pre-existing condition:**<br>Hypertension — 56.6%, obesity — 41.7%, diabetes — 33.8%, coronary artery disease — 11.1%, congestive heart failure — 6.9%<br>Troponin above the test specific upper limit was seen in 22.6% of those tested.<br>Of the patients who died, those with hypertension were **less likely** to have received invasive mechanical ventilation or care in the ICU compared with those without hypertension.<br>Mortality rates for patients with hypertension not taking an ACEI or ARB, taking an ACEI, and taking an ARB were 26.7%, 32.7%, and 30.6%, respectively | This study reported mortality rates only for patients with definite outcomes (discharge or death)<br><br>The case series design cannot address the speculation about the possible adverse, protective, or biphasic effects of treatment with ACEI |
| Zeng JH *et al.* [19], China | Case report | A 63-year-old male | An elevated troponin I (Trop I) level (up to 11.37 g/L) and diffuse myocardial dyskinesia along with a decreased LVEF on echocardiography.<br>Patient improved with antiviral therapy and mechanical life support.<br>However, died of aggravation of secondary infection on the 33rd day of hospitalization | This is the first report of COVID-19 complicated by fulminant myocarditis |
| Inciardi *et al.* [20], Italy | Case report | 53-year-old patient | Acute myopericarditis with systolic dysfunction confirmed on cardiac magnetic resonance imaging — showed increased wall thickness with diffuse biventricular hypokinesis, especially in the apical segments, and severe left ventricular dysfunction<br>The condition developed a week after onset of fever and dry cough due to COVID-19 | The patient did not show any respiratory involvement during the clinical course.<br>Treated with dobutamine, antiviral drugs (lopinavir/ritonavir), steroids, chloroquine, and medical treatment for heart failure |
| Cui *et al*. [21], China | Case report | 55-day-old patient | Abnormal myocardial zymogram on admission and increased troponin I on hospital day 4 indicated myocardial injury<br>The patient also had lung and liver injury | Children with COVID-19 can also present with multi-organ damage and rapid disease changes |
| Bemtgen X *et al*. [22], Germany | Case report | A 52-year-old patient | COVID-19 patient presenting with ARDS plus refractory combined cardiogenic and vasoplegic shock<br>Successfully stabilized after implantation of pVAD plus an ECMO | ECMO and VAD is a labour and resource intensive technique; not always suitable for crowded and burdened ICU |

*These 6 studies have not been included separately in the table

ACEI — angiotensin-converting enzyme inhibitors; ARDS — acute respiratory distress syndrome; ARB — angiotensin receptor blockers; CAD — coronary artery disease; CTPA — computed tomography pulmonary angiograph; DIC — disseminated intravascular coagulation; ECMO — extracorporeal membrane oxygenation; ICU — *intensive care unit; LDH — venous thromboembolism;* LVEF — *left ventricular ejection fraction;* pVAD — percutaneous ventricular assist devices; VTE — *venous thromboembolism*

As the pandemic progresses, our knowledge on this novel infection will evolve. We have sufficient evidence of an increased severity of COVID-19 infection in patients with cardiac diseases and more mortality in patients with COVID-19 related cardiac failure and myocarditis. It is important to alert clinicians of this because it would aid in the timely diagnosis of the cardiac complications. It is also important to acknowledge our poor understanding of the exact pathogenesis because currently, the possible role of angiotensin receptors and the possible long-term effects of this virus are still to be assessed. Trials proving an optimal management strategy have not yet been completed, therefore, the best management that can currently be offered is of a supportive nature. Thus, constant physician vigilance of the clinical presentation of such patients can help in reducing morbidity and mortality until further evidence surfaces.

## Conflict of interest

None declared.

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