The novel COVID-19 disease mainly affects respiratory organs; however, involvement of cardiovascular system is also not uncommon. Cardiac involvement can manifest as myocarditis, heart failure, myocardial infarction, pulmonary embolism, or arrhythmias in COVID-19 patients. This novel Coronavirus enters into the cells of the human body by binding to ACE-2 receptors which are predominantly present on pneumocytes and cardiomyocytes. The damage to myocardium is manifested by the increase in cardiac enzymes such as troponin-I, CK-MB, and NT pro-BNP. Although echocardiogram is an important tool in the cardiac evaluation of COVID-19 patients, its indiscriminate use is discouraged, owing to the risk of transmission to echocardiography service providers, as well as possible risk of contaminating echocardiography equipment. In this article, we discuss the different mechanisms and cardiac manifestations of COVID-19. We also review the current guidelines for echocardiography evaluation of COVID-19 patients as well as current recommendations on safety of echocardiography personnel and equipment against contamination. We also include our experience of two cases in which COVID-19 affliction of heart was strongly suspected, and echocardiography clinched the diagnosis.

Abstract

Cardiac involvement in the coronavirus infection is relatively uncommon in low-risk, younger, asymptomatic patients (< 40 yrs). In middle age/elderly patients, the cardiac involvement progressively increases, and in patients requiring intensive care facilities, with or without ventilator therapy, the prevalence of heart involvement rises steeply and could be in the range of 50 to 60%.

Cardiac Involvement due to Coronavirus Infection can Occur in (Table 1):

1) Patients with preexisting heart disease–coronary artery disease, well-compensated congenital heart disease, valvular heart disease, as well as those in whom there is involvement of the heart in comorbid conditions such as hypertension, diabetes and chronic kidney disease. These patients can undergo worsening and decompensation due to acute stress.

2) Direct/indirect involvement of myocardium (myocarditis) is as follows:

- Direct involvement of the myocardium occurs because of the viral RNA affecting the endothelium of the myocardial vessels, leading to release of troponins (troponin–T and I), causing varying degrees of myocardial dysfunction.

Keywords

- cardiac involvement
- COVID infection
- echocardiography for cardiac evaluation

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Introduction

The Coronavirus pandemic, which started in late 2019 and is still ongoing, has severely stretched and overwhelmed the healthcare infrastructure all over the world. The SARS CoV-2 is transmitted by droplets, which enter the mucous membranes of the patients’ eyes, nose, and mouth. ACE-2 receptors, predominantly present in the lungs, facilitate the entry of the virus into the cells.

Cardiac involvement in the coronavirus infection is relatively uncommon in low-risk, younger, asymptomatic patients (< 40 yrs). In middle age/elderly patients, the cardiac involvement progressively increases, and in patients requiring intensive care facilities, with or without ventilator therapy, the prevalence of heart involvement rises steeply and could be in the range of 50 to 60%.

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• **Indirect** involvement of the myocardium can occur as a result of a severe systemic inflammation, causing release of cytokines/chemokines. These proinflammatory cytokines like tumor necrosis factor (TNF), interleukin (IL)-6, ferritin, C-reactive protein (CRP), and IL-1β are overproduced in response to tissue injury. This phenomenon is called cytokine storm which leads to vascular hyperpermeability, plaque ruptures, and eventually multiorgan failure. This is mediated by activation of monocytes and macrophages.

• The presence of myocardial injury is an independent risk factor associated with increased mortality in COVID patients.5-8

3) Rupture of atherosclerotic plaque on a preexisting critical/noncritical coronary artery disease, causing acute myocardial infarction (MI), usually ST elevated myocardial infarction (STEMI).

• The management of patients with MI could either be using thrombolytic therapy (provided no C/I exist) or be directly referred to a percutaneous coronary intervention (PCI) center. The thrombolytic therapy regimen has the advantage of being cost-effective, immediately available, and more importantly avoiding transmission of infections to the interventional team. However, the advantage of PCI approach avoids unnecessary delays arising from changes in the appearance of classical findings of ECG in STEMI.5-8

4) Myocardial ischemia precipitated by myocardial supply/demand mismatch due to tachycardia, hypoxia, pyrexia, and systemic inflammation which could lead to severe left ventricle (LV) dysfunction.9,10

5) Cardiac arrhythmias varying from benign atrial/ventricular ectopics to life-threatening ventricular arrhythmias like Torsades de pointes, which could occur as a result of the following:

Myocardial inflammation; use of cardiotoxic medications like chloroquine, hydroxychloroquine, azithromycin antiviral drugs; congenital disorders such as Brugada syndrome and long QT; electrolyte imbalance11,12 (→ Table 2).

6) Involvement of pericardium, including myopericarditis, and large pericardial effusions like cardiac tamponade are less frequent manifestations of COVID involvement of the heart.

7) Stress cardiomyopathy is again an uncommon reflection of COVID involvement of the heart, leading to either a classical Tako–Tsubo cardiomyopathy, a more rarer, reverse Tako–Tsubo cardiomyopathy, and nonischemic cardiomyopathy.13,14

8) Cardiac involvement due to pulmonary embolism.

• The prevalence of pulmonary embolism is likely to be in the range of 20 to 30% in patients with COVID pneumonias.

• Significant elevation of D-dimer levels is likely to indicate a high-probability acute pulmonary embolism in a patient with COVID pneumonia and hypoxemia.

• Acute cor pulmonale causing right ventricular (RV) enlargement can occur as a result of pulmonary embolization or severe hypoxemia due to COVID pneumonia itself.15,16

• Recognition of pulmonary embolism is crucial to the management of such critically ill patients, as appropriate use of unfractionated heparin/low-molecular weight heparin could indeed be life-saving.

**Management**

The management of cardiac involvement during COVID infection could be challenging, especially with regard to treatment of hypotension, shock, decompensated cardiac failure, malignant arrhythmia, and electrolyte imbalance. Continuous ECG monitoring in the ICU/telemetric monitoring is an essential component for detecting/managing cardiac arrhythmias. Various cardiac imaging modalities may be required, for example, echocardiography, cardiac CT, and MRI. Critical cardiac care also includes the use of inotropes, vasopressors, antiarrhythmics, diuretics, as well as appropriate management of dyselectrolytemia. Many drugs are presently under trial for specific treatment of COVID-19 (→ Table 3).  

**Use of Cardiac Imaging in the Management of COVID Patients: Guidelines and Protocols**

Echocardiography is the most widely used cardiac imaging modality as it is noninvasive, portable and extremely cost-effective with accurate and immediate results. However, the use of echocardiographic technique exposes
the operator to a high-risk of being infected by the COVID patients; also, there is risk of contamination of the echocardiographic equipment in the COVID ICU (►Table 4).

• Echocardiographic procedure should only be used if there is likelihood of being incremental advantage in the management of the COVID patient with suspected/diagnosed cardiac involvement. Furthermore, echocardiography should be used if it is likely to provide substantial change in management strategy (drug therapy, interventional therapy, or cardiac surgery). Thus, the use of echocardiography should be restricted to the following situations:

1) Hemodynamically unstable patients.
2) Patient with decompensated cardiac failure.
3) Heart murmur.
4) Evaluation of patients with known preexisting cardiac disease.21,22

• However elaborate precautions should be undertaken with regard to protection of the personnel with adequate personal protection equipment (PPE) as well as protection of echocardiographic equipment from contamination. The detailed process of protection of the equipment can be divided into:

A) Before the echocardiographic procedure:

1) Echocardiographic machine is carefully and thoroughly cleaned with sodium hypochlorite solution, including transducers, knobs, touch screen panel, and the monitor of the machine.
2) After drying, the knobs' board, touch screen panel, monitor, and transducer, are then completely covered with transparent polythene, as shown in ►Fig. 1.
3) The main body of the echocardiography machine, the transducer connecting cords, connectors, as well as the electrical wires, are draped in an outer polythene covering, as shown in ►Fig. 1.

B) During echocardiographic procedure on a COVID patient, the outer draping of the body is removed, while the transducers, touch panel, monitor and knobs remain covered with transparent polythene.
C) After the echocardiographic procedure, the echo machine is wheeled back to the echo room, and all the polythene coverings are removed. The entire echocardiographic machine is again cleaned meticulously with sodium hypochlorite solution, and the entire process is then repeated for another examination on COVID/suspected COVID patient.

• High-quality PPE should be provided (as shown in ►Fig. 1), including complete covering of the face, eye-protection glasses, and headgear.

• ECG leads need not be attached to the echocardiographic equipment. The examination should consist of four or five basic views (parasternal LA/SA, Apical 4C/2C, and subcostal or hypochondrial views). The basic aim of the imaging should be:

1. To provide assessment of the LV size and function.
2. To provide assessment of the RV size and function.
4. Assessment of pericardial/pleural effusion.
5. Assessment of fluid status (central venous pressure by inferior vena cava [IVC] size).

### Table 3 Anti-COVID drugs under investigation17-21

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanism of action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine/hydroxychloroquine</td>
<td>Inhibits the production and release of TNF and IL-6</td>
<td>No authoritative RCT</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Antibacterial with antiviral action- Inhibits protein synthesis</td>
<td>No authoritative RCT</td>
</tr>
<tr>
<td>Ritonavir/lopinavir</td>
<td>Anti-HIV drugs–protease inhibitors</td>
<td>No authoritative RCT</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Nucleotide analog which inhibits viral RNA synthesis and replication</td>
<td>Highly promising drug with randomized study, showing significant reduction in duration of active disease among severely ill patients.26</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>Antibody to the IL-6 receptor</td>
<td>Used for cytokine storm</td>
</tr>
<tr>
<td>Ivermectin</td>
<td>Anthelmintic drug which reduces COVID-19 replication in vitro</td>
<td>In vivo effect not confirmed</td>
</tr>
<tr>
<td>Plasma therapy</td>
<td>Antibodies in plasma of recovered patients</td>
<td>Promising therapy undergoing trials</td>
</tr>
</tbody>
</table>

Abbreviation: RCT, randomized control trial.

### Table 4 Appropriate use criteria for echocardiograph22,23

| Only POCUS or FOCUS views are recommended for quick assessment in critical areas | Measurements for LV, RV and LA can be performed offline |
| Use of CT or MRI instead of TEE preferred in cases like LAA clot | Pharmacological stress tests may be preferred over treadmill stress |

Abbreviations: LA, left atrial; LAA, left atrial appendage; LV, left ventricle; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; RA, right atrial; RV, right ventricle.
Cardiac Echocardiography in COVID-19 Infection
Kapur et al.
Journal of Cardiac Critical Care TSS Vol. 4 No. 1/2020

Case 2–A 65-year-old diabetic male, with h/o high fever along with breathing difficulty, was admitted with hemodynamic instability for further management. X-Ray revealed large B/L consolidation. His HR–120/min, BP–80/60 mm Hg, and SPO2–88% at room air. Emergency echocardiography was done with a strong suspicion of myocarditis (►Fig. 3).

Hematological investigations revealed leucocytosis and lymphopenia. COVID test was positive. Echocardiography ruled out any direct or indirect involvement of heart in this patient. Later troponin and NT-proBNP levels were also found to be normal.

Conclusion
Although COVID involvement of the heart is uncommon in young, asymptomatic individuals; it is likely to be a challenging situation in the middle age/elderly population, especially with comorbid conditions. Appropriate management of decompensated, unstable, cardiac...
patients in the COVID ICU is extremely demanding and requires expert management. A judicious use of echocardiography is advised. Hemodynamically, unstable patients may require echocardiography, but in patients with normal troponin levels, its use may be obviated. For performing an additional LV angiogram in patients undergoing coronary angiography or cardiac evaluation by CT scan in patients undergoing CT of the chest for pulmonary embolism, the need of echocardiography can be deferred. However, where patients cannot be transported, bedside echocardiography is an important tool. Provision of high-quality PPE, disinfecting, and draping of the echocardiographic equipment is essential. In the two patients described above, the use of echocardiography was crucial to diagnosis.

Conflict of Interest
None.

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