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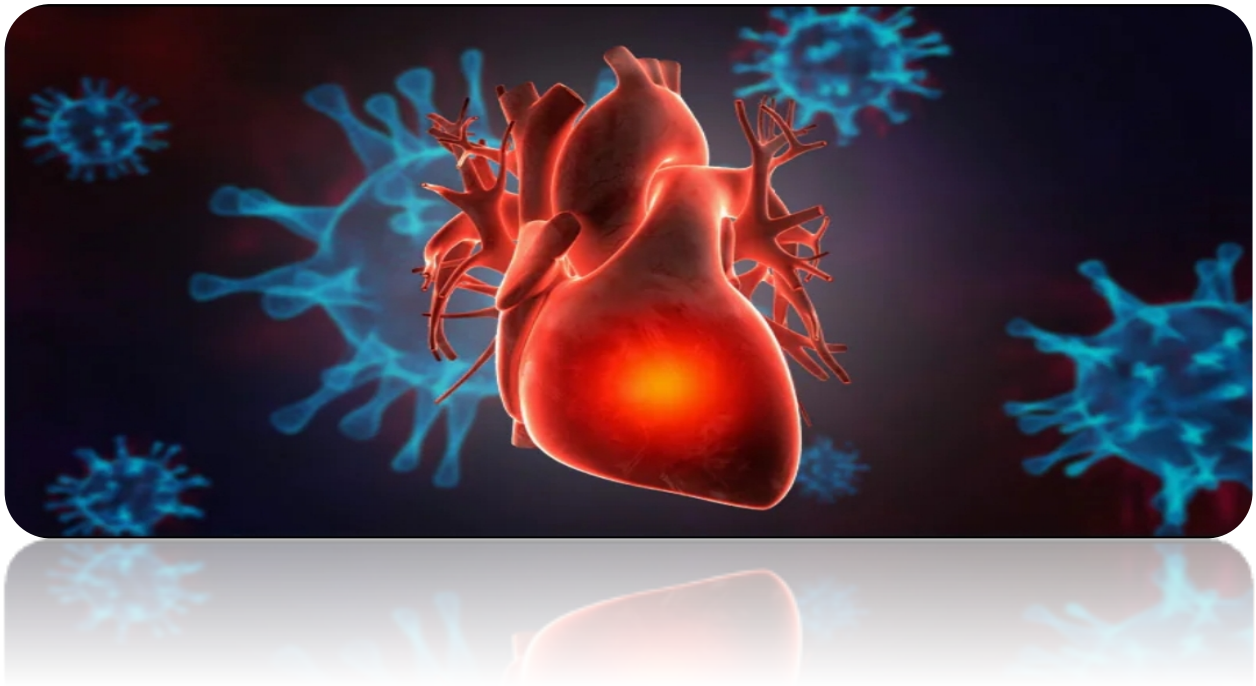
CARDIAC MANIFESTATIONS in COVID19



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INTRODUCTION

Coronaviruses are a large family of enveloped, non-segmented, single-stranded, positive-sense RNA viruses that circulate among animals including camels, cats, and bats. Coronaviruses derive their name from their electron microscopic image, which resembles a crown – or corona .

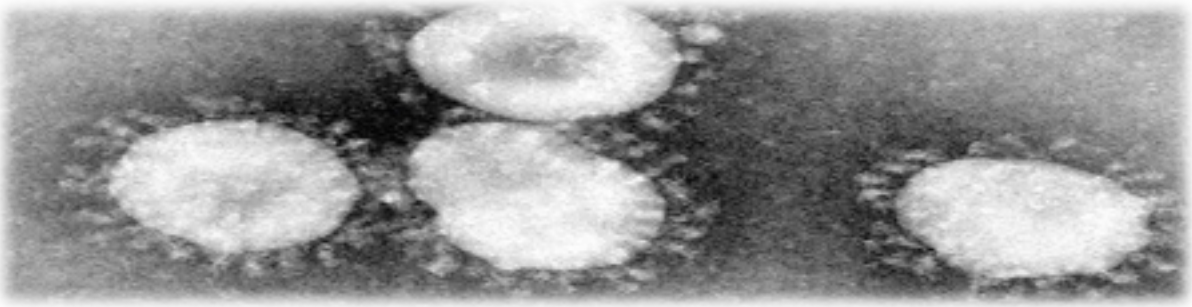


Figure 1. A coronavirus viewed under an electron microscope. Credit: CDC/Fred Murphy.

What is SARS-CoV-2?

On December 30, 2019, a cluster of patients with pneumonia of unknown aetiology. SARS-CoV-2 is a betacoronavirus (an enveloped, single-stranded RNA virus) that shares 79 percent of its genetic sequence with SARS-CoV and has 96 percent homology with the RATG13 coronavirus strain in bats. However, unlike bat coronaviruses, SARS-CoV-2 has a spike protein optimized for high-affinity binding to human ACE2 receptors and a functional polybasic cleavage site at the junction of the spike protein's S1 and S2 subunits (a feature that enhances spike protein cleavage and increases viral infectivity).The disease caused by the SARS-CoV-2 virus is known as coronavirus disease 2019 – or SARS-CoV-2

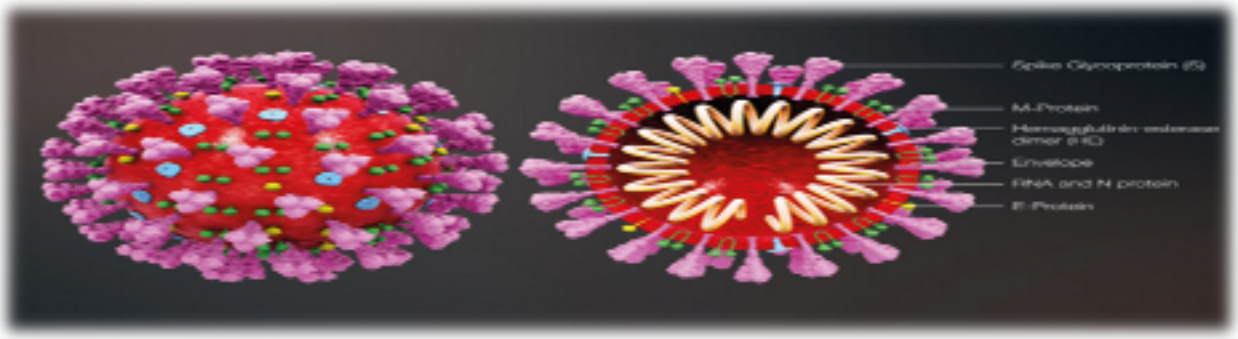


Figure 2. The structure of SARS-CoV-2. Credit: Scientific Animations.

In addition, there are well documented cardiac complications of covid19 in patients with or without prior cardiovascular diseaseCOVID-19 is associated . with notable increases in morbidity and death worldwide. Preexisting conditions, like cardiovascular disease (CVD), diabetes, hypertension, and obesity, are correlated with higher severity and a significant increase in the fatality rate of COVID-19. COVID-19 induces multiple cardiovascular complexities, such as cardiac arrest, myocarditis, acute myocardial injury, stress-induced cardiomyopathy, cardiogenic shock, arrhythmias and subsequently heart failure (HF)

EPIDEMIOLOGY

The infected patients may present with cardiovascular disease (CVD) like acute coronary syndrome (ACS) and congestive cardiac failure (CHF)

Such as in china

The involvement of cardiac factors was recognized early in the pandemic in reports from China. A retrospective analysis of 187 patients treated in a Wuhan hospital between January 23 and February 23, 2020, found that 35% had existing cardiovascular comorbidities such as arrhythmia, coronary disease, and 28% exhibited myocardial injury indicated by elevated troponin T levels.

And World scenario

Beyond China, even higher rates of these comorbidities have been reported. A retrospective case series from Italy presented results from 1,591 critically ill patients with COVID-19 who were admitted to the intensive care unit (ICU): 49% of patients had hypertension, 21% had cardiovascular disease,

In a study from New York between March 2 and April 1, 2020, 1150 adults with COVID-19 were admitted to two hospitals; 257 were critically ill. Of these, 82% had at least one chronic illness, the most common of which were hypertension (63%), diabetes (36%), obesity (46%), and heart disease (19%).In a large case series of 5700 patients with COVID-19 admitted to 12 hospitals in New York, the prevalence of hypertension, and coronary artery disease was 57%, 34%, and 11%, respectively.

Pathophysiology

ACE2 Receptor

SARS-CoV-2 uses its S-spike to bind to ACE2 receptors as the point of entry into the cell. These ACE2 receptors are expressed in type 1 and type 2 pneumocytes and other cell types, including endothelial cells. ACE2 is an inverse regulator of the renin-angiotensin-aldosterone system. Like other coronaviruses, SARS-CoV-2 uses these ACE2 receptors to target the respiratory system primarily.

SARS-CoV-2 and the Immune Response

There are two immune-response phases of COVID-19 disease. Phase 1 occurs during the incubation stage of the disease, during which the adaptive immune system works to eliminate the virus; if any defects occur at this stage, SARS-CoV-2 will disseminate and induce systemic organ damage, with more significant destruction of organs with higher expression of ACE2 receptors, including lung, endothelial cells, the heart, and the kidneys. This massive damage leads to phase 2: severe inflammation in the affected organs. Diabetes, atherosclerosis, and obesity, which are risk factors for cardiovascular disease, downregulate the immune system. These have been associated with a poor prognosis in COVID-19.

Mechanisms of Cardiac Damage in COVID-19

Multiple mechanisms have been suggested for cardiac damage, based on studies conducted during the previous SARS and MERS epidemics and the ongoing COVID-19 epidemic.

➢ Cytokine Release Syndrome:

Cytokine release syndrome occurs in patients with severe COVID-19 infection. Many proinflammatory cytokines are significantly elevated in severe cases, including interleukin (IL)-2, IL-10, IL-6, IL-8, and tumor necrosis factor (TNF)-α. Cytokines play an important role during infection with the virus (phase 1) and during ongoing severe inflammation (phase 2), resulting in acute respiratory distress syndrome (ARDS) and other end-organ damage.

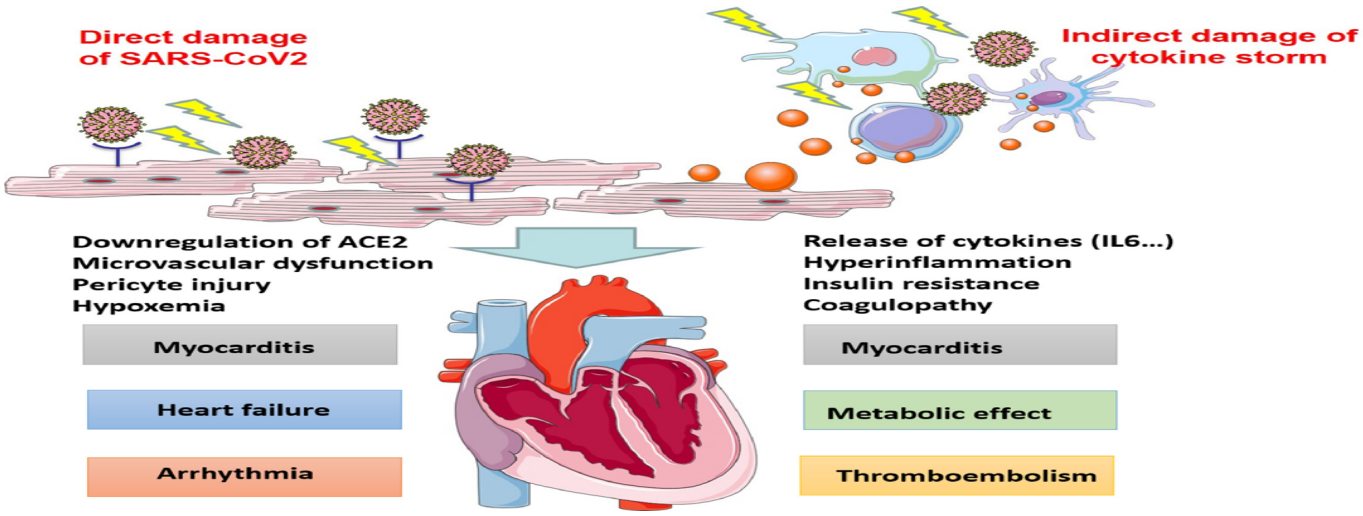
➢ Direct Myocardial Cell Injury

The interaction of SARS-CoV-2 with ACE2 can cause changes to the ACE2 pathways, leading to acute injury of the lung, heart, and endothelial cells. A small

number of case reports have indicated that SARS-CoV2 might directly infect the myocardium, causing viral myocarditis. However, in most cases, myocardial damage appeared to be caused by increased cardiometabolic demand associated with the systemic infection and ongoing hypoxia caused by severe pneumonia or ARDS.

- **Others Possible Mechanisms**

Certain medications such as corticosteroids, antiviral medications, and immunological agents may have cardiotoxic side effects. Electrolyte disturbances can occur in any critical systemic illness and trigger arrhythmias, for which patients with underlying cardiac disease are at higher risk. There is particular concern about hypokalemia in patients with COVID-19, given the interaction of SARS-CoV-2 with the renin-angiotensin-aldosterone system. Hypokalemia is well known to increase vulnerability to various kinds of arrhythmia.



Cardiac Complications with Covid19

❖ Acute coronary syndrome

The term acute coronary syndrome (ACS) is applied to patients in whom there is a suspicion or confirmation of myocardial injury. ACS patients may have either STEMI or non-ST-elevation ACS, which includes NSTEMI or unstable angina. the term acute MI should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise of cardiac troponin.

Definition of MI includes a clinical classification according to the assumed proximate cause of the myocardial ischemia:

- **Type 1:** MI caused by acute atherothrombotic CAD and usually precipitated by atherosclerotic plaque disruption (rupture or erosion).
- **Type 2:** MI consequent to a mismatch between oxygen supply and demand.

With COVID-19 infection, the majority of MIs are type 2 and related to the primary infection, hemodynamic, and respiratory derangement. As such, the primary disorders should be treated, and in most cases the patient can be treated conservatively with regard to coronary disease. If a type 1 infarction is thought to be the primary etiology of the MI, standard therapies can be considered.
In patients with COVID-19, the clinical manifestations of acute CAD are likely similar to those without the virus.

❖ Myocarditis

Human coronavirus-associated myocarditis is known, and a number of coronavirus disease 19 (COVID-19)–related myocarditis cases have been reported. The pathophysiology of COVID-19–related myocarditis is thought to be a combination of direct viral injury and cardiac damage due to the host's immune response.

The prevalence of myocarditis among COVID-19 patients is unclear, partly because the early reports often lacked the specific diagnostic modalities to assess myocarditis. Some argued that up to 7% of COVID-19–related deaths were attributable to myocarditis. However, this was assumed and not based on confirmatory diagnoses of myocarditis and thus may be an overestimate.

Manifestations of SARS-CoV-2 myocarditis varies among different cases. Some patients may present with mild symptoms, such as fatigue and dyspnea, whereas others report chest pain or chest tightness on exertion. Many patients deteriorate, showing symptoms of arrhythmia and acute-onset heart failure with cardiogenic shock. In these severe cases, patients may also present with signs of right-sided heart failure, including raised jugular venous pressure, peripheral edema, and right upper quadrant pain The most emergent presentation is fulminant myocarditis, defined as ventricular dysfunction and heart failure within 2–3 weeks of contracting the virus. The early signs of fulminant myocarditis usually resemble those of

sepsis: the patient often presents febrile with low pulse pressure, cold or mottled extremities, and sinus tachycardia.

The blood tests from myocarditis patients often show elevated levels of lactate and other inflammatory markers, including C-reactive protein, erythrocyte sedimentation rate, and procalcitonin. It is very important to distinguish between sepsis and myositis because the fluid resuscitation of sepsis may exacerbate the myocarditis. The cardiac enzymes level(troponin and BNP) usually elevated in myocarditis.

(ECG) abnormalities commonly seen with pericarditis, such as ST elevation and PR depression, may be observed in myocarditis; however, these findings are *not sensitive* in detecting the disease.

❖ Arrhythmia

it is worthwhile to mention about arrhythmia from previous historic coronavirus epidemics due to SARS-CoV and Middle Eastern respiratory syndrome coronavirus. In a case series of 121 patients diagnosed with SARS-CoV-2, 71.9% were found to have tachycardia independent of hypotension and fever, and 14.9% were found to have bradycardia as a transient event.Tachycardia was not further characterized into arrhythmias, although 1 patient was found to have transient atrial fibrillation. It was noted that the tachycardia persisted in 40% of patients at follow up after discharge. In a case series of 70 patients with laboratory-confirmed Middle Eastern respiratory syndrome coronavirus in 2014 in Saudi Arabia, cardiac arrhythmias including tachyarrhythmias and severe bradyarrhythmia requiring temporary pacemaker occurred in 15.7% of patients

In COVID-19 ,There are well-documented cardiac complications of in patients with and without prior cardiovascular disease and There is growing evidence showing that arrhythmias are also one of the major complications.

The prevalence of arrhythmias and conduction system disease in patients with COVID-19 varies from population to population.The vast majority of patients presenting with a systemic illness consistent with COVID-19 will not have symptoms or signs of arrhythmias or conduction system disease.

Patients may be tachycardic (with or without palpitations) in the setting of other illness-related symptoms (eg, fever, shortness of breath, pain, etc).

While sinus tachycardia is reported secondary to the physiologic response of viral infection ,the development of arrhythmias outside of sinus tachycardia has been reported at a significant rate in COVID-19 patients. Arrhythmias are not an uncommon manifestation of viral infections, and it appears that it is typically initiated by viral myocarditis affecting the cardiac conduction system.

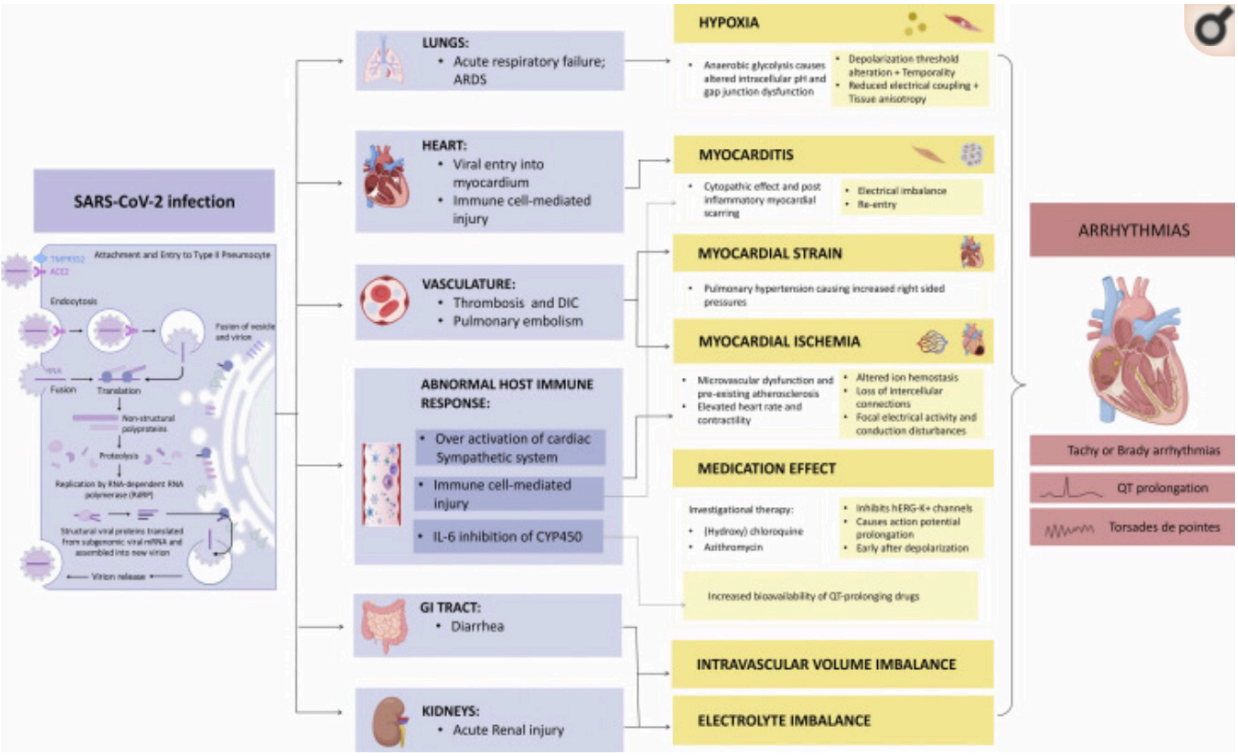
The most common arrhythmia overall in patients with COVID-19 is sinus tachycardia, but the most likely pathologic arrhythmias include atrial fibrillation, atrial flutter, and monomorphic or polymorphic VT.
Also, sinus bradycardia is one of the most common arrhythmia in covid 19 which may persist up to 2 weeks.

Potential risk factors – Patients in whom arrhythmias may be seen include:

1. Patients who present with other cardiovascular complications in the setting of COVID-19 infection, such as myocardial injury or myocardial ischemia.
2. Patient with hypoxia
3. Patients with electrolyte disturbances (eg, hypokalemia)
4. Patient with fever, which can unmask case of cardiac channelopathies such as brugada syndrome
5. Patients who are receiving therapies that prolong the QT interval, which may increase the risk of polymorphic VT.

Arrhythmias are most commonly diagnosed from a combination of vital signs and review of the ECG, ideally a 12-lead ECG, but a rhythm strip can also be used. Tachycardias present with a pulse greater than 100 beats per minute, while most bradyarrhythmias present with a pulse less than 50 to 60 beats per minute.

Most patients in whom COVID-19 is suspected and, in particular, patients with severe disease or in whom QT-prolonging medications will be used, should have a baseline electrocardiogram (ECG) performed at the time of entry into the health care system



❖ Heart failure and cardiogenic shock

Limited data are available on the incidence of HF in patients with COVID19. Patients with COVID19 can have symptoms such as dyspnoea, palpitations and fatigue, which can be attributed to heart failure. In an initial study from China nearly 18.7 per cent of 1099 adult inpatients of COVID-19 had dyspnoea on initial presentation. Acute heart failure ranges from 4.1 to 23 per cent in various studies, and it complicates the clinical course of COVID-19. It is difficult to differentiate the symptoms of acute heart failure from acute respiratory distress syndrome. Increasing level of cardiac troponins and proBNP should raise suspicion regarding myocardial injury in COVID-19.

Patients with a known history of HF may suffer an acute decompensation due to the development of COVID-19 disease.

The heart failure might be the result of exacerbation of preexisting comorbidities whether diagnosed or non, in which the patient is to be old and to have comorbidities such as diabetes , hypertension and coronary artery disease.
At the end of this paragraph, I would like to mention briefly about the several mechanisms of acute heart failure in covid-19:

1. Acute myocardial injury, It may be caused by ischaemia, infarction or inflammation (myocarditis).
2. ARDS, hypoxaemia, acute kidney injury, hypervolaemia, stress-induced cardiomyopathy and a profound systemic inflammatory activation (‘cytokine storm’) could also contribute to acute HF or exacerbation of chronic HF in COVID-19.
3. Sustained/repetitive cardiac arrhythmia may also lead to deterioration in cardiac function.

Diagnostic workup for suspected heart failure includes brain natriuretic peptide, troponin markers, transthoracic echocardiography, and cardiac MRI.
The MRI used to detect the cardiac changes in covid-19 patients with preserved ejection fraction heart failure.
There are several case reports of COVID-19 patients degenerating into cardiogenic shock. The typical echocardiography signs are including biventricular diffuse dysfunction and systemic hypoperfusion without fluid depletionThe hemodynamic assessment was integral to the recognition of cardiogenic shock in these cases.

Cardiac evaluation

- ✓ **Electrocardiogram**

— All patients in whom COVID-19 is suspected should have a baseline ECG performed at the time of entry into the hospital. Ideally, this would be a 12-lead ECG, but a single- or multi-lead ECG from telemetry monitoring may be adequate in this situation to minimize staff exposure to the patient. This will allow for documenting baseline QRS-T morphology should the patient develop signs/symptoms suggestive of myocarditis or an acute coronary syndrome (ACS). Additionally, the baseline ECG allows for documentation of the QT (and corrected QTc) interval. Importantly, QTc will need to be monitored if QT-

prolonging therapies are initiated to reduce the risk of acquired long QT syndrome.

- ✓ **Troponin**

— Cardiac troponin elevation is seen in about 10 to 30 percent of hospitalized COVID-19 patients and is associated with a higher mortality.Most patients with troponin elevation and COVID-19 do not have a clinical presentation suggestive of an ACS.
The optimal use of troponin testing in hospitalized COVID-19 patients without suspected ACS is not known. Many centers obtain a troponin soon after admission in all patients, as it may have prognostic value and may serve as a useful baseline for comparison in patients who subsequently develop manifestations of possible myocardial injury (such as heart failure or arrhythmia) .Other centers limit troponin testing in this setting to patients with a specific indication (such as suspected ACS based on clinical presentation or new onset heart failure), as the clinical value of troponin levels has not been established.

- ✓ **Transthoracic ECHO**

TTE may be useful to evaluate new-onset or acutely worsened heart failure, primarily to rule out new valvular disease or change in ejection fraction; however, a significant wall motion abnormality associated with ACS can also be seen in myocarditis.

- ✓ **Cardiac mri**

Cardiac MRI is unique in its ability to non-invasively identify myocardial edemas and myocardial necrosis, localize sites of inflammation, and assess severity of tissue damage . CMR is currently the gold standard for non-invasive detection and exclusion of myocardial inflammation.

Treatment

COVID-19 infection should be treated to control the progression of the disease, primarily pneumonia .Importantly, if patients have CVD at the same time, they should be aggressively treated.

A treatment protocol should consider the following; general and symptomatic treatment, antiviral treatment, hypoxia, and dyspnea treatment (oxygen therapy, noninvasive and invasive respiratory support), circulatory support therapy for patients in shock, timely use of antibacterial drugs when evidence of secondary infection, treatment for cytokine storm, and

glucocorticoid therapy in severe patients.Supplying oxygen to hypoxic patients *via* nasal prongs, facemask, high flow nasal cannula, or noninvasive ventilation is advisable. Therefore, it is necessary to have extra-corporeal membrane oxygen support and mechanical ventilation. In addition, renal replacement therapy might be necessary in a number of cases.

Management of STEMI cannot be delayed, waiting for the result of COVID-19. If feasible, a dedicated COVID-19 catheterization laboratory is preferabl. The need is to protect HCWs from contracting the infection from a suspected COVID-19 patient.

Patients with acute decompensated heart failure should be managed according to the standard guidelines.

Arrhythmias should be managed as per standard guidelines. Risk-benefit assessment should be done and non-urgent procedures should be postponed and refractory/life-threatening arrhythmias not controlled on medical therapy should be undertaken for electrophysiological study.

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