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Review Article

SARS-COV-2 Infection, COVID-19 Disease, And Impact on Cardiology: A Review of Literature

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Abstract

Coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) has been declared a global pandemic. SARS-COV-2 greatly impacted the global population with its evolving variants. All over, COVID-19 caused a huge global health burden by systemic inflammation, multiorgan dysfunctions, and critical illness with a wide range of clinical manifestations. The cardiovascular (CV) system has been a focus of major morbidity and mortality with COVID-19 disease. Many potential mechanisms have been reported on CV impact by the SARS-COV-2 virus; medications used in the treatment of COVID-19 disease have various effects on the CV system; long-COVID associated morbidity is a growing topic to explore. As knowledge on COVID-19 evolves, this review aims to summarise relevant data on SARS-COV-2 virus infection and COVID-19 disease-related CV morbidity and mortality burden with a focus on potential mechanisms, and impact of long-COVID on the CV system.

Keywords: Arrhythmia; Cardiology; COVID-19; Heart Failure; Long COVID; Mechanisms of Cardiac Involvement; Myocarditis; Post-Acute COVID-19 Syndrome; SARS-COV-2.

Introduction

Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) has a primary impact on the respiratory system. Although the lungs are the main organs involved in coronavirus disease 2019 (COVID-19), systemic inflammation with multiorgan involvement have been reported in the literature. Cardiovascular (CV) complications play a major role in morbidity and mortality associated with COVID-19 especially in individuals with pre-existing CV diseases. These underlying conditions, make patients vulnerable to developing more significant CV injury or unmask the underlying CV conditions. These include cardiac rhythm abnormalities, thrombotic events, destabilization of plaques, endothelial cell injuries, exacerbation or new-onset heart failure etc. The pathways involved in CV injury previously described are myocardial inflammation; cytokine storm, dysregulation of the renin-angiotensin-aldosterone system (RAAS), to name a few. The COVID-19 pandemic has led to increased use of medications like hydroxychloroquine and azithromycin, which can cause cardiovascular complications such as arrhythmias and QT interval prolongation. Additionally, corticosteroids like dexamethasone can contribute to hypertension, fluid retention, and electrolyte imbalances, worsening pre-existing heart conditions [1-3]. Long COVID can result in lingering cardiovascular complications such a postural orthostatic tachycardia syndrome. These prolonged symptoms pose a challenge to patients and healthcare professionals in managing long-term cardiac health [4-5].

The global pandemic caused by the emergence of the SARS-COV-2 virus has led to extensive efforts by the medical community to rapidly expand their knowledge and understanding of the virus and its impact on the human body. This literature is growing every

day. An updated and adequate understanding of the COVID-19 disease and its correlation with the CV system is required for the optimal management of vulnerable patients.

As the COVID-19 pandemic unfolded, cardiovascular consequences began to gain attention early in 2020. Initially, the primary focus was on the respiratory manifestations of the disease. However, as more data emerged, it became evident that COVID-19 also had a significant impact on the cardiovascular system. Over time, researchers observed that patients with pre-existing cardiovascular conditions experienced more severe outcomes and higher mortality rates. Additionally, the pandemic saw an increase in cases of myocarditis, heart failure, arrhythmias, and thromboembolic events in COVID-19 patients, leading to further investigation into the virus's effects on the cardiovascular system. Throughout the pandemic, our understanding of the relationship between COVID-19 and cardiovascular consequences has continued to evolve, highlighting the importance of monitoring and addressing these issues in patient care and management.

The COVID-19 pandemic has had far-reaching consequences on healthcare systems worldwide, including a significant impact on out-of-hospital cardiovascular deaths and serious complications among patients with cardiac diseases. As a collateral effect of the pandemic, there has been a notable increase in non-cardiovascular deaths and complications even among patients not infected with the virus. A study by Santi et al. documented a reduction in emergency department visits during the lockdown period. This study also reported a considerable increase in overall out-of-hospital mortality (43.2%) and cause-specific out-of-hospital mortality related to neoplasms (76.7%), endocrine, nutritional, and metabolic (79.5%), as well as cardiovascular (32.7%) diseases. The pandemic has inadvertently affected patients with cardiac diseases, leading to a surge in out-of-hospital deaths and complications, emphasizing the importance of addressing these unintended consequences and ensuring continuous care for patients with cardiovascular conditions [6].

Epidemiology of COVID-19 disease and cardiovascular complications

It has previously been noted that during seasonal influenza outbreaks, a higher incidence of cases of heart failure, arrhythmias and acute coronary syndrome have been found (7). Data from existing meta-analysis suggests significant incidence of such cardiac complications in hospitalized COVID-19 patients. Myocardial injury and heart failure are the most common complications, with pooled incidence of myocardial injury going up to 30% (19-42 95% CI) and of heart failure up to 22.34% (14.05-33.60 95% CI) [8-9]. Koeppen et al in their meta-analysis noted very high incidence of cardiac arrhythmias which was comparable to other common complications, 24% (14-36 95% CI) [8]. Patients whom had pre-existing cardiovascular diseases (CVD), had overall poor outcomes [10]. A pooled meta-analysis revealed the patients with pre-existing CVD had a significant increase in fatal risk , OR = 2.72; 95% CI 2.35–3.16; I2 = 66%, P < 0.00001) [11]. However, in a study examining COVID-19 patient outcomes in relation to pre-existing cardiovascular (CV) disorders, significant findings emerged. The study included 5133 patients, with 1174 (22.9%) having a history of CV disease. It was observed that 1178 (34.6%) patients died, and 920 (17.9%) experienced a cardiovascular event. After adjusting for variables such as age, sex, race, body mass index, smoking history, and comorbidities, pre-existing CV disorders were linked to a 1.15 times higher odds of death. However, no independent association was found between pre-existing CVD and cardiovascular events. Interestingly, the study concluded that it was the CV risk factors, rather than the CV disorders themselves, that played a significant role in determining the outcomes for critically ill COVID-19 patients [12]. Cases of COVID-19 related myocarditis have been reported in literature. SARS-COV2 has been associated with a higher incidence of myocarditis which was possibly related to COVID-19 directly infecting the myocardium [13-14]. A systematic review described ST- segment elevation in 161 COVID-19 patients, of which 83% had obstructive coronary artery disease with a 30% overall in hospital mortality [15]. Right ventricular dysfunction (RVD) was another very common complication with a reported pooled prevalence of 20.4% (95% CI 17.1-24.3%; 95% PI 7.8-43.9%). Presence of RVD increased the overall likelihood of all-cause mortality (OR 3.32, 95% CI 1.94-5.70) This was reported on a meta-analysis of 3813 patients by Corica et al [16]. See in (Table 1) reports pooled incidence of cardiac complications in hospitalised COVID-19 patients.

Myocardial injury was used to describe a patient with at least one cardiac troponin (cTn) concentration exceeding the 99th percentile upper reference limit. An arrhythmia represented any rhythm deviating from normal sinus rhythm with proper atrioventricular (AV) conduction. Heart failure was defined as a clinical syndrome characterized by symptoms and/or signs stemming from a structural and/or functional cardiac anomaly, which is supported by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion. Acute coronary syndrome (ACS) definition included a range of clinical manifestations consistent with acute myocardial ischemia, including unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Cardiac arrest was defined as the abrupt halt of cardiac function, rendering the individual unresponsive, without normal respiration, and lacking any signs of circulation. Lastly ST-segment deviation was referred to as the displacement of the ST segment above or below the baseline, which is frequently indicative of myocardial ischemia, injury, or infarction.

Study	Total Patients	Myocardial Injury (MI)	Arrhythmia	Heart Failure (HF)	Acute Coronary Syndrome	Cardiac Arrest	ST‐segment Deviation
Zhao et al (15)	3044	21.2% (12.3-30.0% 95% CI)	15.3% (8.4-22.3% 95% CI)	14.4% (5.7-23.1% 95% CI)	1.0% (0.5-1.5% 95% CI)	-	-
S K Kunutsor and J A Laukkanen (16)	5815	16.3% (11.8-21.3; 95% CI)	9.3% (5.1-14.6; 95% CI)	17.6% (14.2-21.2; 95% CI)	6.2% (1.8-12.3 95% CI)	5.7% (2.7-9.6 95% CI)	-
M Koeppen et al (7)	4281 (ICU patients)	30% (19-42 95% CI)	24% (14-36 95% CI)	5% (0-15 95% CI)	-	-	-
M Sahranavard et al (8)	4157	17.85% (13.18-23.72 95% CI)	10.11% (5.12-19.0 95% CI)	22.34% (14.05-33.60 95% CI)	-	-	-
S Garcia-Zamora et al (17)	12499	-	10.3% (8.4-12.3 95% CI)	-	-	-	8.7% (7.35-10.0 95% CI)

Note: All percentages are given along with their 95% confidence intervals (CI).

Table 1: Pooled Incidence (along with Confidence Interval) of Cardiac Complications in Patients Hospitalized with COVID-19

Potential Mechanisms of Cardiovascular System Involvement In COVID-19

Direct Effect on Myocardium and Dysregulation of Renin-Angiotensin-Aldosterone System

A study for cellular targets of SARS-COV-2 and expression of Angiotensin-Converting Enzyme 2 (ACE2) revealed that alveolar type 2 cells and macrophages, in the lungs, are the primary targets of the virus, followed by cardiomyocytes (19% of cells) as the next most likely targets in the human body [17]. A structural study on SARS-COV-2 virus has demonstrated that the virus enters the host cell through the attachment of the transmembrane spike protein (S protein) to the ACE2 receptor by the receptor-binding domain (RBD) of the virus [18]. Compared to the previous SARS-COV virus, certain characteristics of the SARS-COV-2 support a very efficient cell entry of the virus. For example, the novel virus has a high affinity of the RBD to bind to the ACE2 receptor, enables pre-activation of the spike reducing its dependence on the target host cell enzymes, and utilizes a hidden nature of the RBD in the spike [19]. Furthermore, SARS-COV-2 has 10-to-20-fold stronger affinity towards the ACE2 compared to the previous SARS-COV virus [18]. An autopsy study of 336 cases reported that the SARS-COV-2 virus was detected in 47% of post-mortem myocardial samples (2). Another study on COVID-19 autopsy with a focus on cardiac pathology showed poorer outcomes and higher mortality in patients with detectable myocardial SARS-COV-2 virus [20]. These findings are suggestive of the direct myocardial effect of SARS-COV-2. However, significant research on the pathophysiology of the myocardial damage by the SARS-COV-2 virus is still needed.

ACE2 has a protective role by negative regulation of the RAAS cascade. ACE2 converts angiotensin 2 into angiotensin 1-7 which then binds to the MAS receptor and provides a protective role with anti-inflammatory, anti-hypertrophy, and vasodilatory actions. These properties are essential in maintaining the pathophysiological balance of the body. Entry of SARS-COV-2 virus into the cell causes downregulation of surface expression of ACE2 receptors. Such downregulation leads to an elevated level of angiotensin 2 which then binds to the angiotensin 1 receptor leading to negative consequences such as vasoconstriction, pro-inflammation, fibrosis, hypertrophy, enhanced reactive oxygen species generation, and multi-system dysfunction in COVID-19 disease [21-23]. Such physiological imbalance in response to viral infection and COVID-19 disease may potentiate the CV complications in patients with no prior history of CV disease. Additionally, these factors can worsen existing CV condition.

After considering a wide range of factors, it has been observed that using ACE inhibitors and ARBs may decrease the likelihood of contracting COVID-19. The use of ACE inhibitors or ARBs does not seem to increase the chances of requiring ICU care significantly. However, differences among different ethnic groups suggest that the effects of ACE inhibitors/ARBs on the susceptibility and severity of COVID-19 may be specific to certain ethnicities, and this requires further investigation [24]. This confounding argument on the use of ACE inhibitor and ARB

(angiotensin receptor blocker) with COVID-19 has generated clinical confusion. Currently, clinical trials and cardiology societies recommend continuing the use of ACE inhibitors and ARBs if a patient is already tolerating them [25-28].

Endothelial Dysfunction and Thrombo-inflammatory Disease State

The endothelium has an important role in maintaining vascular homeostasis by producing vasodilators and vasoconstrictors, inflammatory and anti-inflammatory, procoagulants and anticoagulants, fibrinolytics and antifibrinolytics, oxidizing and antioxidizing, and other agents. When this equilibrium is lost, consequences occur which lead to a thrombo-inflammatory disease state (3). Autopsy studies reported evidence of the presence of SARS-COV-2 viral particles in the myocardium and demonstrated higher severity of capillary dilation, microhaemorrhages, and microvascular dysfunction in cases with detectable viral load [20]. Myocyte necrosis with microthrombi as a major mechanism (64% cases) was reported in a study of 40 autoptic cases which also reported a different nature of COVID-19 disease-related microthrombi constituents (high fibrin and terminal complement component) compared to intramyocardial thrombi from COVID-19 negative cases and epicardial coronary artery thrombus of COVID-19 positive and negative cases [29].

Once SARS-COV-2 virus enters the vascular endothelium, it activates changes that lead to endothelial cell structural and chemical changes. SARS-COV-2 can stimulate the Neutrophil-derived extracellular traps (NETs) which potentiate extrinsic-intrinsic coagulation pathways and generate reactive oxygen species [30-31]. A study noted significant elevation in markers to detect NET in COVID-19 hospitalized patients, and also demonstrated that COVID-19 sera are potent stimulators of NETosis (program for the formation of NETs) when added to control neutrophils [31].

Hyperactivation of the platelets has been reported in COVID-19 which also contributes to cytokine storm and an associated thrombo-inflammatory state. This study also demonstrated more efficient aggregation and adherence of platelet to collagen surface when originated from COVID-19 patients [32]. Overall, COVID-19 disease is a pro-NETotic state and potential triggers are activated platelets, neutrophils, endothelial cells, and inflammatory cytokines, etc [31]. The inflammatory damage from the above potential causes increases vascular permeability secondary to enlarged endothelial intercellular gap junctions and extravasation of immune cells into the myocardium which leads to reactionary changes causing myocardial edema, myocyte necrosis, and microthrombi formation which are reported findings in reviews of myocardial autopsy [2,29].

These suggest a direct role of SARS-COV-2 virus in endothelial dysfunction and related CV complications in COVID-19 disease. Considering the above evidence, treatment options directed towards the endothelium and NET formation can have a potential therapeutic implication. Further research on such targets in high-risk patients can be fruitful.

Dysregulation of The Immune System with Cytokine Storm

Extensive evidence shows that cytokine storm in COVID-19 is related to the severity of disease and may be a driver of myocardial injury. Elevated levels of Interleukin (IL) 1, IL-2, IL-6, IL-7, IL-8, IL-10, Interferon (IFN) gamma, tumour necrosis factor (TNF) alfa, vascular endothelial growth factor have been detected in COVID-19 systemic disease [33-34]. These inflammatory markers activate more innate immune cells (neutrophils, macrophages, monocytes, natural killer cells) and adaptive immune cells (CD4 and CD8 T cells) in order to produce sustained inflammatory cytokines by bone marrow stimulation. Overproduction of cytokines particularly IL-2, IL-6, IFN gamma, TNF alfa trigger macrophage activation, erythrophagocytosis (i.e., Hemophagocytic Lymph histiocytosis- HLH), can dysregulate the coagulation cascade, resulting in thrombotic complications, increased capillary leak, and endothelial dysfunction [34]. Hyperactivation of platelets has been reported in COVID-19 disease and a study has shown the direct contribution of platelets to the plasma cytokines load which suggests a role of platelets in cytokine storm [32]. Overall, these dysregulated inflammatory states result in critical illness and multiorgan dysfunction including cardiac dysfunction. Cytokine storm can lead to direct or indirect cardiotoxicity with effects such as conduction abnormalities, hypotension, heart failure, fulminant myocarditis, LV remodelling, etc [1,35]. Literature suggests the deleterious cardiovascular effects, of TNF alfa is mediated through activation of the sphingomyelinase pathway (immediate pathway within minutes) followed by nitric oxide-mediated blunting of beta-adrenergic signalling (delayed pathway in hours to days) which can lead to progressive LV dilation; of IL-1 is mediated at least partly through the nitric oxide and indirectly through activation and release of IL-18 [35], CANTOS trial has demonstrated positive CV outcomes with IL-1b inhibition [36]. IL-6 association with athero-thrombotic complications and aneurysm formation was demonstrated in a study but the role of direct inhibition of IL-6 in preventing vascular event rates still needs to be tested [37].

Acute Respiratory Distress Syndrome causing right heart strain and dysfunction

The lungs are the primary organs involved in COVID-19 disease, and severe disease causes acute respiratory distress syndrome (ARDS). ARDS causes various pathophysiological changes in cardio-pulmonary mechanics which affect the right ventricular (RV) function. In ARDS, pulmonary circulation is affected through hypoxia-induced pulmonary vasoconstriction, interstitial edema, microvascular thrombosis, etc. Such changes

increase pulmonary artery pressures which directly impacts the RV afterload. Increased resistance in the pulmonary vascular system affects RV ejection, venous return (preload), and left ventricular function due to ventricular interdependence. In ARDS, lung-protective ventilation strategy- high positive end-expiratory pressure (PEEP) is recommended. High PEEP also increases pulmonary vascular resistance, intrathoracic pressure, and RV afterload which further contributes to RV dysfunction. Therefore, ARDS itself and positive pressure support modalities in the treatment of ARDS can have deleterious consequences on RV function. Adjusting the settings of such treatment modalities according to RV tolerance, maintaining a balance of adequate PEEP and limited plateau pressure, avoiding hypoxia, and hypercapnia is the key in management [38-39].

The prevalence rate of echocardiographically evident RV dysfunction in ARDS varies from 22 to 50% according to the measurements used to evaluate it with a higher sensibility of . (38). RV FAC (fractional area change) and RV VTI (velocity time integral) [40].

Dysautonomia

Dysautonomia is a disorder caused by dysfunction of the autonomic nervous system which affects the balance between the sympathetic and parasympathetic nervous systems and ultimately impairs the function of the heart and other organs. Various case series report cardiovascular symptoms such as postural light-headedness and tachycardia, orthostatic hypotension, or postural hypertension (by hyperadrenergic state) as primary disability and can be presented even after a few weeks as long-COVID morbidity [41-42]. Dysautonomia could be a result of direct virus effect on autonomic pathways, para-infection or immune-mediated. A recent article provided insights on the possibility of sympathetic and cytokine storms together along with RAAS system activation as final pathways in the development of dysautonomia with COVID-19 [43].

A case series of 20 patients with dysautonomia reported 85% of the patients still experienced significant disability impacting personal and professional life 6 to 8 months after COVID infection [41].

Further research is still needed on this topic considering a wide scale of the possible impact on COVID survivors due to the global scale of the pandemic.

Medications for COVID-19 and its impact on the CV system

Both the novelty of COVID-19 disease and the rapidity of the global pandemic spread of SARS-COV-2 infection, challenges researchers and clinicians toward developing new medications and repurposing already approved medications to fight against COVID-19 disease. However, such trial medications have potential side effects and interactions in the human body which can negatively impact the cardiovascular system function. Some of the widely used medications for COVID-19 in current times are covered here (and in table 2) with references on data demonstrating CV complications.

Remdesivir (anti-viral medication) – hypotension, arrhythmia-mainly bradycardia, QTc prolongation [44-46]

Tocilizumab/ Sarilumab (IL-6 inhibitors) - hypertension [47], hyperlipidemia [47-48]

Steroids (immunosuppressant medication) - hypertension

Lopinavir/ Ritonavir (anti-viral medication) - QTc prolongation [46,49], cardiac contractile dysfunction, hyperlipidemia [50]

Hydroxychloroquine and Azithromycin – QTc prolongation, arrhythmias such as torsades de pointes, and sudden cardiac death [46,49,51]

Ivermectin (antiparasitic medication) – unknown

Favipiravir (anti-viral medication) - QTc prolongation [46]

Ribavirin (anti-viral medication) – bradycardia, and causes hypomagnesemia and hypocalcemia which potentially can impact cardiac function [52]

Medication	Mechanism of action in COVID-19 disease	Potential cardiac adverse effects	References	Number of Participants	Publication Date
Remdesivir	RNA-dependent RNA polymerase inhibitor. Thus, terminates the viral RNA transcription.	hypotension, arrhythmia-mainly bradycardia, QTc prolongation	44-46	44: 2604 45: 1086 46: 2403	44: 2021 45: 2020 46: 2021
Tocilizumab/ Sarilumab	Monoclonal antibodies which competitively inhibits binding of the IL-6 to its receptor IL-6R. Thus, prevents signal transduction and dampens the inflammatory response.	hypertension, hyperlipidemia	47-48	47: 513 48: 3986	47:2021 48: 2015
Steroids	Anti-inflammatory medications	hypertension	-	-	-
Lopinavir/ Ritonavir	Protease inhibitor. Thus, reduces the virus replication and release from the host cells.	QTc prolongation, cardiac contractile dysfunction, hyperlipidemia	46, 49, 50	46:2406 49: Not reported 50: Not reported	46:2021 49: 2021 50: 2013
Hydroxychloroquine (HCHQ) and Azithromycin (AZ)	HCHQ- interfere in endocytic pathway, prevent ACE2 glycosylation, promote blockade of sialic acid receptors to interfere with SARS-COV-2 life cycle. AZ- potential antiviral and immunomodulatory actions.	QTc prolongation, arrhythmias such as torsades de pointes, and sudden cardiac death	46, 49, 51	46: 2403 49: Not reported 51: 4112	46: 2021 49: 2021 51: 2021
Ivermectin	Anti-viral effect likely through inhibiting IMPα/β1-mediated nuclear import of viral proteins.	unknown	-	-	-
Favipiravir	RNA-dependent RNA polymerase inhibitor. Thus, terminates the viral RNA transcription.	QTc prolongation	46	46: 2403	46: 2021
Ribavirin	Decreases the expression of TMPRSS2 (transmembrane serine protease 2), which affects viral cell entry into host cell. Also, acts as viral polymerase inhibitor. Thus, affects viral replication.	bradycardia, and causes hypomagnesemia and hypocalcemia which potentially can impact cardiac function	52	52: 306	52: 2012

Table 2: Medications for COVID-19, mechanism of action and its potential cardiac adverse effects

Myocardial Damage from Hypoxia/ Demand and Supply Mismatch

COVID-19 pneumonia is a significant morbidity of the SARS-COV-2 virus. Impairment of pulmonary function is negatively related to systemic oxygen supply due to hypoxia from the ventilation-perfusion mismatch. As described in the above sections, microvascular endothelial dysfunction and micro thrombosis compromise the oxygen supply to the tissue. On the other hand, a higher circulating level of cytokines and related inflammation from COVID-19 systemic disease increases the end organ metabolic needs. Plus, stress-related physiological reflex tachycardia reduces the available ventricular filling time which potentially impairs the cardiac output and systemic as well as coronary circulation [53]. Type 2 myocardial infarction occurs when the myocardial oxygen demand/supply ratio is altered in association with higher cardiometabolic demand [53]. Overall, the combination of hypoxia from acute respiratory illness, high demand state from COVID-19 systemic disease, impaired tissue oxygen supply from micro and macrovascular complications from COVID-19 lead to a mismatch in end-organ oxygen demand/ supply chain which ultimately potentiates the CV compromise.

Impact of long-COVID on cardiovascular system

Most people with COVID-19 disease recover, but some may continue to experience lasting symptoms for weeks or months after their initial infection. The term long-COVID was coined for such clinical condition that has a beginning but not a clear end.

Several studies reported a high incidence of long covid that varies from 39% (4) at 77.1%after 9-12 months after the infection [54].

More than 50 symptoms have been described in long-COVID. Fatigue is the most common reported symptom followed by cough, headache, attention disorder, hair loss, dyspnoea etc [5,55].

In long-COVID, pooled prevalence of chest pain has been reported as 10% (from five studies with 30 to 180 days of overall follow up time from discharge) [55], other meta-analysis study (5) reported most common cardiovascular symptoms are chest pain/discomfort 16%, resting tachycardia 11%, palpitations 11% (studies defined the long-COVID as symptoms ranging from 14 to 110 days from viral infection). Signs of myocarditis (1%) and arrythmia (0.4%) were reported rarely (5).

Imaging studies show evidence of persistent cardiac involvement weeks after initial infection. Echocardiography study [56] at 4 to 12 weeks post-acute COVID-19 infection, in patients without pre-existing CV conditions reported presence of pulmonary hypertension, RV and LV dysfunction, diastolic dysfunction (DD) in post-acute COVID-19 phase, with higher prevalence in patients with more severe pulmonary injury and who were examined earlier after initial phase. It is not clear if DD is associated with high blood pressure. Same study also reported more prevalence of DD in obese population (14%), majority of these population also showed LV hypertrophy and it was mostly examined between 9 to 11 weeks after initial infection. Pericardial evaluation showed presence of pericardial effusion in early phase (4 to 8 weeks after initial infection) and higher prevalence of thickened pericardium in subjects with late evaluation. Another recent study [57] with echocardiographic CV evaluation within 4 to 12 weeks of initial infection in adult patients less than 55 years of age without baseline CV comorbidities showed higher prevalence of pulmonary hypertension, cardiac DD in patients who required inpatient care during acute infection compared to outpatient only. PH was characterized by a resting right ventricular systolic pressure (RVSP) of 36 mm Hg or more when pulmonary valve stenosis is not present. There was no association between pulmonary embolism and electrocardiographic PH in patients with COVID-19.

MRI based studies demonstrated cardiac changes in long-COVID patients. Myopericardial inflammation was demonstrated on cardiac MRI (94 days median time interval between COVID-19 diagnosis and MRI), it showed higher pericardial enhancement, effusion; as well as higher native T1-native T2 which were also associated with severity of symptoms [58]. A study showed 25% patients with severe post COVID syndrome had myocarditis compared to 12% patients with moderate syndrome (141 days median time interval from initial symptoms to assessment) and overall 19% prevalence of myocarditis and 9% systolic dysfunction [59].

As described in this article, acute SARS-COV-2 infection causes wide spectrum of cardiac functional and structural abnormalities which potentially can last for long time after acute phase of the COVID-19 disease. Considering these, it appears that CV complications in these patients can at least explain some of the long-COVID symptoms such as fatigue, chest pain, palpitations, dyspnoea, low exercise capacity etc. which are associated with poor quality of life in many patients due to long lasting symptoms.

Conclusion

SARS-COV-2 infection and COVID-19 disease has tremendously impacted the global health care system. Evolving variants of the novel virus is causing COVID-19 disease of various clinical significance. From the clinical perspective, knowledge about the mechanisms of CV involvement and clinical-pathological-radiological signs of CV disease in COVID-19 and long-COVID would provide better understanding, early diagnosis, and treatment opportunities in this population. Our review summarises the updated and important aspects of CV involvement

by SARS-COV-2 in acute phase and in post COVID phase. The medical fraternity has been spending enormous efforts towards research, new literature, and a better understanding of the virus's impact on the human body, disease progression and associated CV complications. With this, there will be many other evolving views, perspectives and newer data in upcoming future expanding our horizon of understanding of current disease.

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