Review Article

In Depth Review of COVID-19 Effect on CVS

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ABSTRACT

Corona virus disease 2019 (covid-19) is global pandemic affecting 185 countries and > 30,00,000 patient worldwide as of April 28,2020 COVID-19 is caused by severe acute respiratory syndrome corona virus. Which invades cells through the angiotensin – converting enzyme 2 receptor. Among patient with COVID-19, there is a high prevalence of cardiovascular disease and > 7% of patients experience myocardial injury from the infection (22% of critically ill patients). Although angiotensin – converting enzyme 2 serves as the portal for infection, the role of angiotensin – converting enzyme inhibitor or angiotensin receptor blockers requires further investigation. COVID-19 poses a challenge for heart transplantation, affecting donor selection. Immunosuppression and post-transplant management. Primary cardiac manifestation includes acute myocarditis, myocardial infarction, arrhythmia and abnormal clotting. The disease does not discriminate but increasing age & the presence of comorbidities are associated with severe form of the disease and poor outcomes. While our knowledge of COVID-19 continues to rapidly expend, this review highlights recent advances in our understanding of the interaction between COVID-19 & the cardiovascular system. Management of acute COVID-19 cardiovascular syndrome should involve a multidisciplinary team including intensive care specialists, infectious disease specialists and cardiologists. Clinical and diagnostic details of cardiovascular involvement in these patients a mostly limited to biochemical markers. Cardiovascular drugs the cardiac effect of therapeutic agent on the illness continue to be under investigation with an increasing number of patients newer promising therapies and ongoing clinical trials the exact mechanisms & extent to which this risk. Factors contribute to outcomes will be clearer in the future.

Keywords: Angiotensin, COVID-19, Cardiovascular, Infection, Pandemic.

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INTRODUCTION

Corona virus 2019 (COVID-19) is a highly transmittable human respiratory tract infection caused by the newly discovered RNA β-coronavirus called acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Corona virus has suffered from previous epidemics, such as SARS-CoV and Middle East Respiratory Syndrome (MERS)-CoV. Since the discovery of the index, which is linked to the oceans and the aquaculture market in Wuhan, Hubei province, China, in December 2019 [2], the disease has spread to more than 200 countries. As of 29 May 2020, the number of cases in the US was 1,719,827, including 101,711 deaths[3]. The first case of COVID-19 was reported in the US on January 30, 2020, and, since then, more than 1.5 million cases have been reported. Given the high morbidity and mortality caused by the disease in the short term and the high rate of transmission, the World Health Organization (WHO) announced the COVID-19 epidemic on March 11, 2020[4].

Timeline of corona virus infection affecting humans

1965:Tyrrell and Bynoe1 identified a virus named B814, 2002–2003: Severe acute respiratory syndrome (SARS), 2012: Middle East Respiratory Syndrome, 2019–2020: Covid-19 (the illness caused by SARS-CoV-2 infection), First reported case to the WHO Country Office in China on 31 December 2019, On 20 January 2020, the CDC confirmed a positive test for 2019-nCoV, by RT-PCR, in an individual in the US, In a meeting on 30 January 2020, per the International Health Regulations (2005), the WHO declared the outbreak was a Public Health Emergency of International Concern, On 11 February 2020, the WHO Director-General announced that the disease caused by this new CoV was 'COVID-19', WHO raised the threat to the CoV epidemic to the 'very high' level on 28 February 2020, On 11 March 2020 WHO declared COVID-19 a pandemic.

The mortality rate indicates a strong age gradient at risk of death. In the United States, the highest death toll for ≥85-year-olds (10% to 27%) was followed by people aged 65 to 84 (3% to 11%) and <1 % for all ages[5]. In addition to age, the severity of the disease is related to the presence of comorbidities. Most importantly, for those with severe COVID-19, an increase in cardiovascular conditions was reported[6]. China's National Health Commission reported that 35% of patients diagnosed with COVID-19 had high blood pressure and 17% had heart disease (CHD)[7]. Therefore, patients with coronary heart disease (CVD) can

present with serious diseases that can lead to myocarditis, vasculitis, or cardiac arrhythmias[8]. Clinical presentation of this disease especially pulmonary, with computed tomography of the chest which contributes to the diagnosis and help with the severity and severity of the disease[9,10]. Reports of cardiac manifestations of COVID-19 infection increase[11,12].

Similar to SARS and MERS, it is believed that SARS-CoV-2 has moved from the bat to the central host (probably the Malayan pangolin, which shares 91% nucleotide ownership) and to humans [13] (Fig 1). SARS-CoV-2 infection is caused by the binding of excess viral protein to the angiotensin-converting enzyme 2 (ACE2) receptor after the activation of spike protein by transmembrane protease serine 2[14].

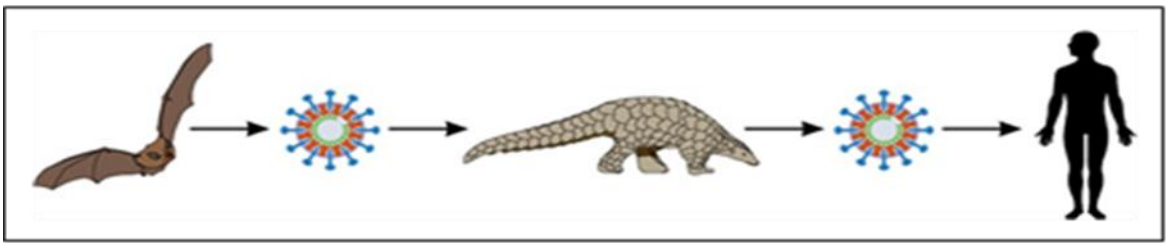

Figure 1: Pathway of severe acute respiratory syndrome corona virus 2 to humans[13]

Early reports suggest the most common symptoms are fever (88%) and dry cough (67.7%), which are shared with many other viral syndromes. In this review, we briefly discuss the pathogenesis, clinical manifestations, and diagnosis of COVID-19, cardiovascular effects, medication, treatments and managements of COVID-19 and future complications and implications with future discussion.

Pathogenesis

SARS-CoV-2 uses the enzyme-converting angiotensin enzyme 2 (ACE 2) to enter target cells[15,16].

In the heart, ACE 2 is found mainly in the carotid endothelium, in the heart myocytes, and in the smooth muscle cells of the myocardial vessels. Although ACE 2 is highly depleted in the heart, the exact mechanism of heart damage is not yet fully developed it is understandable[17]. The two different mechanisms of cardiac injury discussed so far in COVID-19 are non-ischemic myocardial injury and myocardial ischemia[18-20]. Among these, non-ischemic myocardial injury has been reported extensively in several studies.

The various types of non-ischemic myocardial injury published in the literature include [i] cytokine storm, as marked by elevated signaling signals such as C-reactive protein, ferritin, procalcitonin, etc., [ii] secondary to hemo phagocytic lympho histiocytosis following infection, [iii] viral myocarditis with progressive myocardial infarction [iv] hypoxia- induced cardiac myocyte apoptosis[18,17,21].

Although Ischemic injury, despite its submission, has not been discontinued the evidence so far. Systemic inflammation, inflammation- induced prothrombotic state and increased shear pressure following increased coronary blood flow have been stopped to reduce plaque rupture causing features of acute coronary syndrome[18,17]. Other cardiovascular and thought to cause side effects are dyselectrolytemia (such as hypokalemia) and cardiovascular drugs that work on the Renin Angiotensin-Aldosterone axis (such as angiotensin receptor blockers), and other drugs including statins, various antiviral agents, steroids, hydroxychloroquine, and azithromycin[18,22,23]. However, these reports are undependable and do not have a solid scientific basis to be used as current clinical evidence(Fig 2). represents the 3 main factors that contribute to cardiac injury in patients with COVID 19. Older patients can have a significant impact on cardiac injury as shown in the picture, which puts them at higher risk of poor outcome.

Cardiovascular enzymes involved in critical troponin I (cTnI) are elevated in all of the above-mentioned processes following heart damage regardless of the procedure[21,24,25]. Uncontrolled, persistent, and dysfunction of the immune system leading to excessive cytokine release have been demonstrated with the effects of high plasma levels of Interleukins (IL-2, IL-7), granulocyte colony system lating factor, IgG-produced protein, chemokine ligand 3 and tumor necrosis factor alpha among patients admitted to intensive care units with COVID-19.

Patients with heart damage have also been reported to have high plasma levels of procalcitinin, ferritin, D-dimer, active C-protein (CRP) and leukocytes[15,21,25]. Among these high cTnI, and elevated cTnI is a diagnostic condition and predict the outcome in patients with cytokine-related cardiac injury. In several studies, this cytokine-related heart attack has also been reported to predict outcomes including acute respiratory syndrome (ARDS), severe kidney injury, severity of illness, the need for intensive care unit admission and death[17,19,21,26].

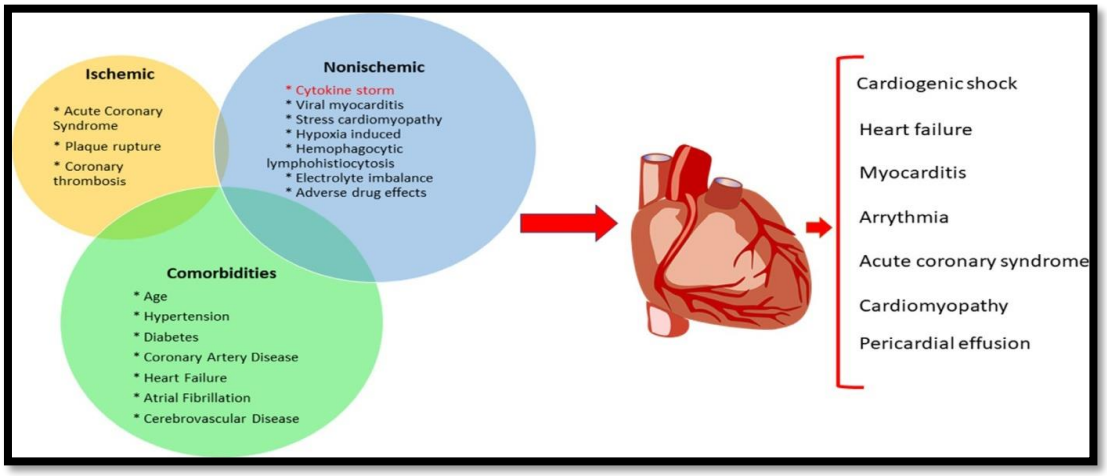

Figure 2: Mechanism and patterns of cardiac injury in COVID-19

The exact pathogenesis of cardiac involvement is not entirely clear. Increases in cardiac biomarkers, including troponin T, have been shown to correlate with inflammatory symptoms, suggesting that myocardial damage may be related to primary inflammation[27]. Several mechanisms of heart damage may be at play, including direct myocardial injury by the virus itself, hypoxic damage associated with respiratory failure, indirect damage associated with cytokines responding to systemic response, myocardial infarction (MI) due to subsequent fracture , prothrombotic condition produced by severe systemic inflammation, and ischemia from myocardial infarction-seek imbalance (Fig 3). Direct ACE2 cardiac injury is also possible. ACE2 receptors are expressed in pericyte heart and endothelial cells, and animal data suggest that their direct inactivation by viral infection or secondary inflammation may reduce MI [28,29].

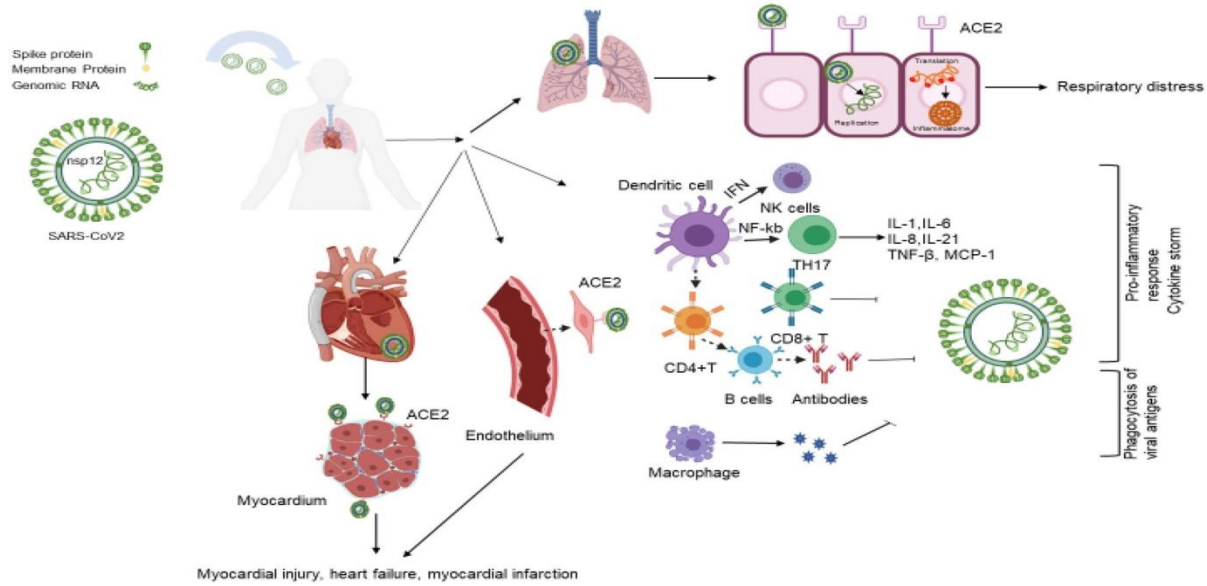

Figure 3: Diagram of the COVID-19 structure and route of infection

Manifestation

The median incubation period of COVID-19 was estimated to be 5.7 days, with 97.5% of patients developing symptoms within 12.5 days of exposure[30]. The most common symptoms are unexplained, including fever (88%), fatigue (70%), dry cough (67.7%), anorexia (40%), and myalgia (35%). Anosmia and dysgeusia have also been reported as significant and specific symptoms. Respiratory symptoms such as rhinorrhea are very common. Intestinal symptoms, including nausea and diarrhea are also uncommon[31,32]. Preliminary experience from China suggests that approximately 81% of infected patients contract serious illnesses, and serious illnesses increase by 14%. Acute respiratory pneumonia (ARDS) is a very common symptom. Serious illness with septic shock and multiple organ failure was reported in 5% of patients[33].

Cardiac manifestation

Pericardium

Pericardial effusion has been reported in patient. A study involving 90 patients who experienced variability in computed tomography (CT) of the chest reported

pericardial discharge in 1% of patients[34]. Their study did not find this practice or the appearance of a new pericardial discharge following a picture made in 6 days[26]. One study reported that about 5% of patients had pericardial effusion[10,35]. The same is shown in autopsy shows pericarditis in patients[36]. There are various reports of pericardial depletion recorded in the echocardiography of COVID-19 patients[37].

Myocardium

Myocardial infarction mainly presents as a major cardiac injury within 8 12% of patients. This has been defined by elevated serum cardiac biomarkers, abnormal discovery of abnormalities in electrocardiogram, or abnormal detection in echocardiogram of an infected patient and cardiogenic shocks have also been reported[18,17,21]. In patients with infected myocarditis, restoration of cardiac structure and function is known. Only mononuclear filtrates were reported in myocardial tissue autopsy when high viral load was determined. There have been reports of fulminant myocarditis with high troponin and improvement in left ventricular function following intravenous immunoglobulin and steroids, as well as normal troponins activation[37,38].

Cardiovascular Effect

Previous epidemics have been associated with a significant increase in the incidence of myocarditis, cardiomyopathy, HF, MI, arrhythmias and sudden cardiac death[39-41]. It was therefore unexpected to see higher CV incidence rates in those with COVID-19. On the other hand, the presence of existing heart conditions appears to increase the risk of complications, including death, in COVID-19 patients. As reported in a meta-analysis of patients approved for COVID-19, the incidence of CV (CVD) cases was 16.4% in non-intensive care unit (ICU) patients, and tripled in those in need of ICU[42]. In the following sections, we highlight the various comorbidities of the CV and the disruptions reported so far on COVID-19(Table 1).

Table 1: Summarizing published case studies showing baseline cardio vascular comorbidities in COVID-affected patients

Author	Place of study	Date accepted/ published	Total no. of patients	Mean age, years	% of male patients	% of female patients	% of HTN	% of DM	% of CVD/CAD	% of other cardiac diseases[a]
Chenet al.[30]	China	January 2020	99	55.1	68	32	NA	12	40	NA
Huanget al.[13]	China	January 2020	41	49	73	27	15	20	15	NA
Zhanget al.[31]	China	February2020	140	57	50.7	49.3	30	12.1	5	3.6
Wangetal.[32]	China	March2020	339	69	49	51	40.8	16	15.7	NA
Wuetal.[33]	China	March2020	280	43.1	53.93	46.07	NA	12.14[d]	20.4	NA
Zhouet al.[17]	China	March2020	191	56	62	38	30	19	8	NA
Chenet al.[34]	China	March2020	274	62	62.4	37.6	34	17	8	NA
Lianget al.[35]	China	March2020	1590	48.9	57.3	42.7	16.9	8.2	3.7	NA
McMichaeletal.[36]	USA	March2020	101	83	31.7	68.3	67.3	31.7	60.4	NA
Caoet al.[37]	China	April2020	102	54	52	48	27.5	10.8	4.9	14.7[b];17.6[c]
Shaoet al.[38]	China	April2020	136	69	66.2	33.8	30.2	20	11	NA
Richardsonetal.[39]	USA	April2020	5700	63	60.3	39.7	56.6	33.8	11.1	6.9
Goyaletal.[40]	USA	April2020	393	62.2	60.6	39.4	50.1	25.2	13.7	7.4
Grassellietal. [41]	Italy	April2020	1591	63	82	18	49	17	21	NA

*CAD:*coronaryarterydisease,*CVD*cardiovasculardisease,*DM*diabetesmellitus,*HTN*hypertension,*Na*notavailable,
[a]Othercardiacdiseasesincludecongestiveheartfailure,acutecardiacinjury,arrhythmia, [b]Acute cardiac injury, [c]Arrhythmia,
[d]Endocrine system disease

Myocardial Damage

Severe myocardial injury during viral illness may be attributed to an increase in certain biomarkers, electrocardiographic changes, or new cognitive features of dysfunctional heart function. Previous experience of Middle Eastern respiratory infections, acute respiratory infections (SARS), COVID-19, and non-SARS coronaviruses suggest that coronavirus can cause acute myocarditis[43-48]. In COVID -19, the frequency and differentiation patterns of troponin release in the context of clinical presentation of type 1 or 2 myocardial infarction, myocarditis, or cytokine / cardiomyopathy-related stress are not well defined. Anecdotal reports described cases of severe myocardial injury characterized by elevated troponin heart rate associated with elevated ST segment or depression in ECG and angiography often without coronary artery disease or identified lesions[47,49]. This Preliminary data suggest that the main cause of myocardial injury of this phenotype is myocardial injury in the absence of epicardial coronary artery thrombosis.

In addition, myocarditis, systemic cytokine-mediated, stress-related cardiomyopathy, or microvascular thrombosis may present a pattern of acute myocardial injury(Fig 4).

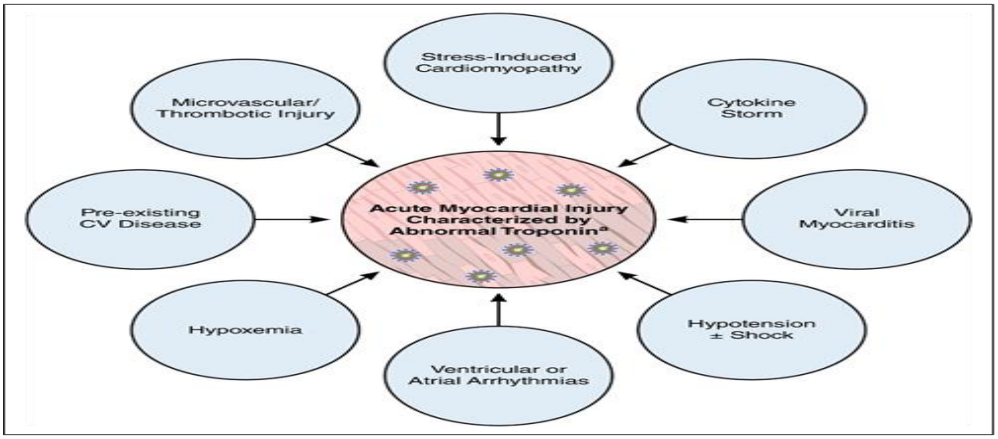

Figure 4: Prospective mechanisms of myocardial injury COVID-19 CVS.

Myocardial infarction, demonstrated by high cardiac biomarkers, was recognized among the first cases in China. In the above-mentioned study of 138 patients in COVID-19 hospitals in Wuhan, China, heart damage(new troponin [hs-cTnI] or new ECG or echocardiographic abnormality) was present in 7.2% of patients and 22% of patients in need of ICU care[50]. A report from the Chinese National Health Commission reported that 12% of patients without known CVD had elevated troponin levels or cardiac arrest during hospitalization[51]. Particularly, hs-cTnI was> 99th percentile with a high reference point in 46% of survivors compared to 1% of survivors[52](Fig 5).

Severe myocardial injury as tested for troponin release alone appears to be a major complication for patients in hospitals with COVID-19, especially patients in need of intensive care. Analysis of a series of 52 critically ill patients in China with COVID-19 revealed myocardial injury (high-sensitivity cardio troponin I [cTnI]> 28 ng / L) in 29% of patients[53]. A report of 416 patients hospitalized with COVID-19 noted that% 20% (82 of 416) patients had severe myocardial injury (cTnI> 0.04 µg / L) and patients with myocardial injury were older and had a higher burden of disease comorbid. Myocardial Injuries are associated with high mortality observed continuously after initial correction and clinical interventions[54]. A report from a multidisciplinary Chinese study containing data containing 191 patients in hospitals with COVID-19 detected myocardial injury (cTnI> 28 ng / L) in 1 of the 95 (1%) surviving patients compared to 32 of the 54 (59%) non-surviving patients[55].

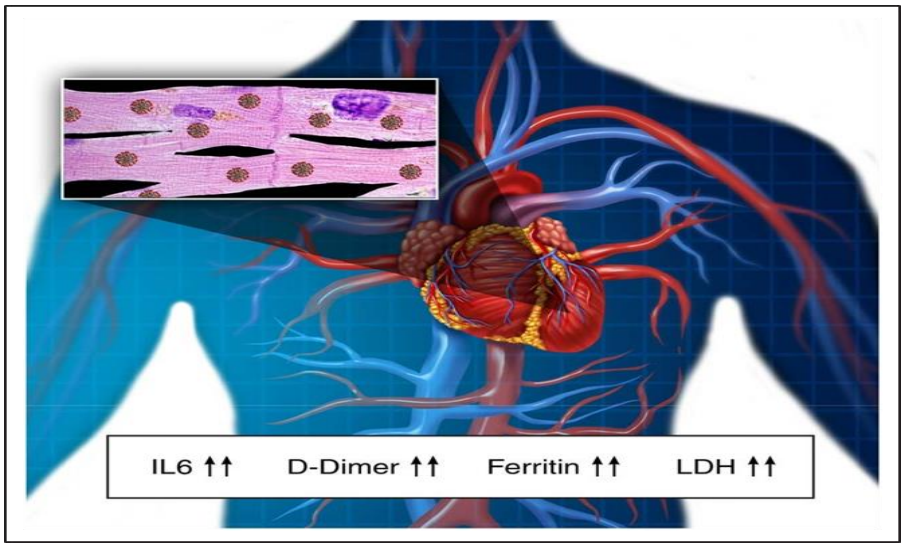

Figure 5: Mechanism of myocardial injury from COVID-19

Additional reports from Wuhan indicate that a significant number of obese patients also had high transaminases, lactate dehydrogenase, creatine kinase, D-dimer, serum ferritin, interleukin-6, and prothrombin time, all of which suggest that strong inflammatory mediators with a similar cytokine profile in cytokine release syndrome[54,55]. This star of inflammatory cytokines has similarities to chimeric antigen receptor T-indened cytokine release syndrome, leading to a significant increase in interleukin-6 and interferon- γ[56]. For ACovCS, it is unclear whether such elevated cytokine levels contribute to or contribute to myocardial injury, ventricular dysfunction, and elevated

heart troponin. Additional studies, including the collection of endomyocardial tissue by biopsy and autopsy studies, are needed to explain the pattern and value of ACovCS associated with acute myocarditis compared to normal myocardial injury caused by systemic cytokine dysregulation.

Coronary Ischemia/Infarction

Coronary involvement and ischemia have been identified, including ST-elevation myocardial infarction (STEMI) and non-elevation myocardial infarction (NSTEMI), in many ways describing coronary artery involvement. As ACE2 is expressed in endothelial visit cells, direct viral infection can lead to plaque instability and type 1 MI. Plaque instability and fractures may also result from a strong inflammatory response in the third stage of the disease. COVID-19 can also increase type II MI by seeking ischemia as patients become more ill. Hypoxia The second involvement of the lungs, as well as fever and tachycardia adjacent to sepsis, further heart function. Coronary artery involvement may continue to be produced by micro angiopathy also described. Such involvement of the small vessel may be caused by systemic vasculitis or micro embolization from ACS or the spread of hypercoagulability that impairs blood flow[57].

Cardiac Arrhythmias

Cardiac arrhythmias known to occur in patients with COVID-19[58,59]. Ventricular arrhythmias, as well as acute myocarditis, may present as early clinical manifestations. Electrolyte imbalances caused by COVID-19 contact with the RAAS system may lead to increased hypokalemia risk of developing arrhythmias[59]. In the study above, the total incidence of arrhythmias was 16.7% in patients with COVID-19. This incidence was higher in patients requiring ICU admission (44.4%) compared with those who did not require ICU admission (8.9%)[60]. Unfortunately, the types of arrhythmias in these patients have not yet been published. Guo et al reported that in 187 patients with COVID-19, 27.8% had elevated troponin levels and in this group, fatal arrhythmias were more prevalent than those with normal troponin levels (11.5% vs 5.2%)[61]. Thus however, the higher incidence of arrhythmias in patients with COVID-19 may be due to electrolyte and hemodynamic disorders in which there is severe inflammatory stress. Patients with inherited or acquired arrhythmias should be monitored while receiving supportive treatment as some drugs may promote arrhythmogenic activity[58].

For example, drugs, such as chloroquine and hydroxychloroquine, are being investigated in the treatment of COVID-19 can cause an increase in the QT interval which leads to the formation of malignant arrhythmias. In addition, if both chloroquine or hydroxychloroquine are given with drugs that inhibit the enzyme CYP3A4, this can greatly increase the risk of temporary increase. QT[58]. Therefore, continuous ECG monitoring is required in these patients.

Arrhythmias leading to cardiac arrest deserve special mention. Cardiopulmonary resuscitation (CPR) with chest compressions is a very high risk of developing aerosolization of the virus, and a small number of caregivers should be inside the room, with complete PPE. In order to reduce prolonged exposure, CPR devices may be considered, and every effort should be made to prioritize temporary placement in a closed area by anesthesiologists so that the duration of any aerosolization maturation is kept to a minimum. While waiting for intubation, air / bag / mask with filter is recommended. The choice of intubation tools should be determined by the expected success rate, with preference given to devices with the highest pass rate. Video laryngoscopy should be used where possible to ensure the rapid and effective management of the procedure, and that not connected to a closed-circuit breaker should be objective[62].

Venous Thrombosis

It is known that inflammatory countries increase the risk of venous thromboembolism (VTE). It is likely that COVID-19 patients with respiratory failure, comorbidities and mobility problems will be at greater risk for VTE. One study in a 138-patient facility assessed VTE risk using the Padua prediction scale (Table 2)[63,64]. According to laboratory findings, the study found that D-dimer was higher in those admitted to the ICU compared to non-ICU patients (414 vs 166mg / L; P <.001)[60]. The study included 179 patients with COVID-19, The D-dimer level ≥0.5mg / L was present in 76.2% of non-survivors compared to only 47% of survivors. Non-compliant analyzes highlighted this as a risk-related risk (death severity: 3.474 [1.152-10.481]); P = .027)[65]. In unhealthy patients, VTE is a major concern. In a recent study with 81 patients with COVID-19, Cui et al showed that 20 improved VTE lower extremity, in which eight patients died. Aging, low lymphocyte levels and high D-dimer were risk factors. Therefore, the risk of VTE should be assessed especially in older patients with comorbidities and medications that should be given according to local guidelines.

Table 2: Risk evaluation of Padua model.

Padua risk assessment model	
Features	Score
Active cancer	3
Previous VTE	3
Reduced mobility	3
Known thrombophilic condition	3
Recent trauma and/or surgery (≤1mo)	2
Age(≥70y)	1
Heart and/or respiratory failure	1
Acute MI or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1

Obesity (BMI≥30kg/m^2)	1
Current hormonal therapy	1

Abbreviations: BMI ;body mass index; VTE, venous thromboembolism

COVID-19 in patients with CVD

CVD was the most common form of attack on patients with COVID-19 that preceded SARS and MERS. In SARS, the prevalence of DM and CVD was 11% and 8%, respectively, and the presence of comorbidity increased the risk of death by 12[66,67]. DM and high blood pressure was common in ≈50% of cases -MERS; CVD was present in ≈30% of patients[68]. In Group 1 of 191 patients from Wuhan, China, any abnormalities were present in 48% (67% of underweight), high blood pressure in 30% (48% of underweight), DM in 19% (31% of survivors), and CVD in 8% (13% of non-survivors) [52]. In a cohort of 138 hospital patients with COVID-19, comorbidities were the same (46% in total and 72 in total). % of patients in need of ICU care], such as cardiac comorbidities: high blood pressure at 31% (58% of patients in need of ICU care), CVD in 15% (25% of patients in need of ICU care), and DM at 10% (22% of patients in need of ICU care)[50]. A group of 1099 patients with COVID-19 reported that 24% had complications (58% among those with intubation or death), with 15% hypertension (36% among those with intubation or death), 7.4% DM (27% among those with intubation or death), and 2.5% with heart disease (9% among those with intubation or death)[69]. Data from the National Health Commission of Chin a showed that 35% of patients diagnosed with COVID-19 had high blood pressure and 17% had coronary heart disease[51]. Recent meta-analysis In eight studies from China including 46,248 infected patients showed that the most common interactions were hypertension (17% ± 7% [95% CI, 14% to 22%]) and DM (8% ± 6% [95% CI, 6% to 11%]), followed by CVD (5% ± 4% [95% CI, 4% to 7%])[70]. The structure of these organizations is not yet clear. Possible explanations include that CVD is more prevalent in patients with age, immune function, or higher ACE2 levels, or patients with CVD that may be exposed to COVID-19.

COVID-19 Target Tissues

Most of the previous experience of myocardial injury associated with a viral infection can be found in the data from diseases unrelated to coronaviruses. For example, clinical syndromes containing COVID-19 suggest a higher rate of myocardial infarction compared with those observed with coxsackie virus disease. The outbreak of SARS coronavirus 1 (SARS-CoV-1) in 2003, the SARS epidemic, led to a vigorous investigation into our understanding of SARS-CoV-2. A study in SARS-CoV-1 revealed that the virus produces many spike (S) proteins on the surface of the virus envelope that are important for transmitting infection[71]. These proteins bind to S1 subunit to the enzyme that converts angiotensin 2 (ACE2) expressed in host cells, but simply binding to ACE2 is not enough for cellular infection. cells to perform sensitive protein priming leading to mutation, cellular invasion, and cell infection[71,72]. Investigations into SARS-CoV-2 have confirmed the importance of the S1 protein binding to ACE2 in targeted cells and the expression of TMPRSS2 protease of host cellular infection[73].

Methods that interfere with S1 subunit binding, ACE2 binding, or TMPRSS2 protein activity are potential therapeutic targets. This hypothesis was tested by testing the effect of antibodies on the S protein found in the recovery serum of patients with SARS-CoV-2. Antibody administration reduced cell-based penetration in a concentrated manner, indicating effective inhibition of viral entry into the in vitro cell line[73]. In addition, anti-ACE2 antibodies administration has been shown to prevent SARS-CoV-1 and SARS-Duplication of the CoV-2 virus in the in vitro cell-based regulation, and further support receptor significance as needed for cellular infiltration[71,73]. In addition, preliminary pre-use ACE2 management reports repeat -1 and SARS- CoV-2 in vitro[74]. Finally, serine protease inhibitors TMPRSS2 have been effective in reducing cellular penetration into SARSCoV-1 and SARS-CoV-2 in the in vitro model[73]. 3 different possible therapies aimed at reducing cellular penetration and pathogenesis. Results from these small in vitro studies suggest that anti-ACE2, TMPRSS2 inhibitors, and S1 protein subunits may reduce the spread of the virus to host cells, although further study is required.

Given the critical nature of ACE2 infection, the distribution of ACE2 expression has the potential to define infected tissue and traumatic thought processes. ACE2 is found mainly in type 1 and II lung alveolar epithelium; pericytes; cardiomyocytes; enterocytes in the small intestine, including the duodenum, jejunum and ileum; and endothelial arterial and venous cells[75-77]. Examination of patients killed by SARS-CoV-1 confirmed the presence of the virus within ACE2-expressing cells, including bronchiolar and alveolar epithelial cells, renal cells tubular epithelial cell, mucosal and crypt epithelial intestinal tract cells, as well as cardiomyocytes[78]. Analysis of histological samples of lung tissue in patients with COVID-19 reveals a pattern of injury similar to that reported by SARS-CoV-2[79]. Although this data is extremely limited to COVID-19 in the present case, they provide evidence for the concept of direct damage to tissue cells with ACE2 expression. Targets for SARS-CoV-2 myocardial cells can include pericyte, cardiomyocytes, fibroblasts, and immune cells such as macrophages.

Antihypertensive Medications

It is estimated that 15-30% of COVID-19 patients have hypertension (HTN). Indeed, a meta-analysis (n = 46,248) including eight studies from China showed that the most common heart rate was HTN (17 ± 7%, 95% CI 14-22%)[80]. The expression of the ACE2 receptor is similar to adipose tissue and non-adipose tissue, but as obese people with adipose tissue in the body, they may have a growing number of receptors. Although some have reported that obesity is a risk factor for COVID infection, more data is

needed to determine whether obese individuals are at greater risk[81].

Given the widespread use of ACE inhibitors (ACEI) and angiotensin receptor blockers (ARBs), as well as the major role of ACE2 receptors in disease pathogenesis, there has been some concern about the use of these drugs in COVID-19 patients. Animal data have supported that chronic use of ARBs enhances the expression of the ACE2 receptor, and higher expression of ACE2 has potential anti-CV effects[82]. Zhang et al. recently published a retrospective study, which included more than 1128 adult patients with COVID-19 and found a lower risk of all causes of death through the use of ACEIs / ARB patients compared to non-ACEIs / ARB patients[83]. Jarcho et al. highlighted three recently published studies, which show no evidence of an increased risk of infection or mortality in COVID patients affected patients who continue these medications. Other recent studies have shown similar confirmation[84]. Based on the available data, most major community guidelines recommend stopping the suspension of ACEIs / ARBs in patients who are already taking these drugs or starting these medications in newly diagnosed patients[85].

Diagnosis

Historically, patients are more likely to be diagnosed with acute myocarditis when they have <30 days of symptoms with abnormal troponin and cardiac magnetic resonance imaging that meets the revised Lake Louise 2018[86]. Non-COVID-19 cases, endomyocardony biopsy in complete presentation to produce a rare presentation of eosinophilic, hypersensitive, and giant-cell myocarditis[87]. However, in the case of COVID-19, such an approach may not be possible due to patient instability, process risk, and risk of exposure to health professionals, especially if the results of biopsy would not change clinical management. Patterns of myocardial delay delays associated with acute myocarditis are also described in the improved classification of ECG-gated multi detector computed tomography in non-COVID-19 cases[88].

This may be a rapid, invalid screening test for myocardial disease in four patients. COVID-19 completes a computed tomography scan for non-cardiac reasons and represents an opportunity for investigation. With the introduction of COVID-19 highly contagious and alarming, management-related priorities and diagnostic options for a patient with ACovCS include reduced staff / patient exposure, a goal that can be helped by reducing patient evaluation and referral diagnostic procedures, especially those that do not directly affect patient management. Another consideration is limiting the tests that require the final room cleaning required by the referral of a patient because that procedure may add significant delays in diagnostic tests for some patients. Such strategies can lead to increased diagnostic uncertainty but are unlikely to magnify short-term adverse outcomes in patients who do not have full submissions. For example, in patients known as high troponin, if type 1 myocardial infarction can be diagnosed for clinical reasons, then biopsy is unlikely to change clinical management as soon as possible if clinical syndrome is caused by myocarditis, cytokine injury caused by myocardial infarction, or type 2 myocardial infarction. Therefore, a standard endomyocardial biopsy in patients with active COVID-19 with abnormal cardiac biomarkers, whether complete or non-complete presentation, is debilitating. This strategy is in line with the latest recommendations of the American College of Cardiology[89].

Cardiac involvement in many studies is based on higher cardiac biomarkers. High levels of troponin sensitivity have been reported consistently in patients with cardiac involvement[11,15]. The details of electrocardiography and echocardiography have not been reported in the same way in many studies. Although details of multiple heart findings and anatomy marks are available, this has been used as a participatory marker[25].

Electrocardiography

Details of EKG detection in patients with COVID-19 are limited. In a study involving 416 patients in only 82 hospitals (19.7%) they were thought to have had a heart attack. Among those with a heart attack only 27% of people received EKG. Of these 63% EKGs were produced in combination with high cardiac enzymes. These EKGs showed no bias-specific cardiac injury including T wave compression and conversion, ST segment suppression, and Q presence waves[25]. Another important change in EKG has been an increase in ST segment III and AVF and sinus tachycardia[17,21]. We recently detected a patient with heart failure and reduced the fraction of ejection presenting EKG evidence of new initiation of atrial relation and rapid ventricular rate.

Biochemical markers

Biochemical symptoms including high lactate dehydrogenase (LDH), creatinine kinase (CPK), creatinine kinase MB (CK-MB), D dimer, high sensitivity troponin are reported to be elevated in patients with autoimmune-related injuries. COVID-19patients with elevated LDH, CK-MB, and D-dimer were reported to be at greater risk of needing ICU care[19,21,25]. The most sensitive troponin has been used consistently in all studies to report heart damage[11,21,24].

Chest X- ray

Most x-rays on the chest have prominent pulmonary parenchymal features as well as insignificant cardiac effects. However, in a 37-year-old man presenting with coronavirus fulminant myocarditis, the first chest x-ray showed results affecting cardiomegaly. Interestingly, after one week, at the time of removal the chest x-ray showed abnormal silhou cardiac[26].

Echocardiography

In most studies, the number of patients diagnosed with echocardiography is scanty. Prescribed reports have been described of finding in transthoracic echocardiograms in patients with suspected cardiogenic shock. Abnormalities

reported in patients with evidence of COVID-19 complete myocarditis include myocardial dyskinesia, left ventricular enlargement, decreased left ventricular output, high pulmonary hypertension, reduced IVC collapse, and pericardial effusion[21,37,38]. Ventricular width, wall size, and function, 1-2 weeks after treatment of patients with clinical improvement[37].

Computed tomography

Cardiac involvement in chest CT is also rare and can be seen only in 1 5% of patients[26]. Patiently presenting with high-resolution ST-segment, CT coronary angiogram performed did not show evidence of coronary stenosis[37]. Similarly, 18F-FDG PET CT studies of 4 patients did not show increased cardiac output. However, it reported mediastinal, right hilar, and supraclavicular lymphadenopathy[90].

Cardiac magnetic resonance imaging (MRI)

Cardiac MRI showed evidence of wall enlargement with biventricular hypokinesis and dysfunctional infrared ventricular dysfunction in asymptomatic 53-year-old patient. Distribution of gadolinium development beyond the biventricular wall has also been noted in the sequence of critical phase detection, fulfilling the conditions for acute myocarditis. Pericardial circumferential recognition was noted, enlarged by 12 mm around the right cardiac chambers[91].

These diagnostic studies may be completely avoided or delayed until recovery from COVID-19 unless the patient degrades clinically and exacerbates hemodynamic instability, shock, ventricular arrhythmias, or elevated or rapidly elevated troponin (Fig 6).

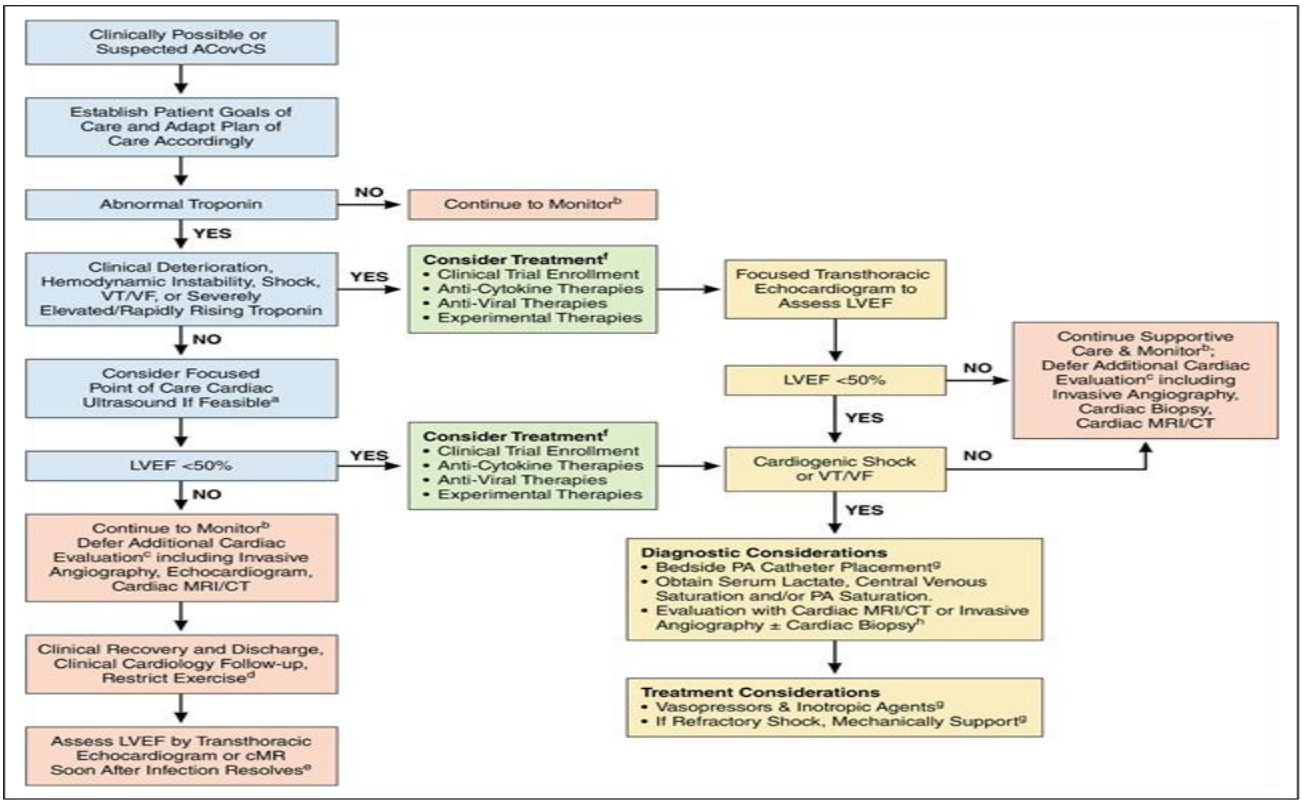

Figure 6: Management of acute COVID-19 cardiovascular syndrome with acute myocardial injury.

Treatment

Many drugs have been supportive. Various agents include antivirals, hydroxychloroquine, azithromycin, IL-6 receptor antagonist, and many other agents have been reported as potent therapies[18,17.] The mortality benefit of these agent is yet to be established in clinical trials. The reported results following the administration of corticosteroids and immunoglobulin in the arteries are inconsistent. Concerns about the progression of statins, angiotensin receptor blockers, ACE inhibitors in patients with previous cardiac comorbidities are awaiting further clinical evidence[22]. Meanwhile, concerns are deepening with the increase in QTC and the risk of cardiac arrhythmias in patients receiving hydroxychloroquine, and azithromycin for treatment[20].

Measures to prevent the best strategies in COVID-19. Vaccines and monoclonal antibodies against SARSCoV-2 are advancing, but alternative therapies, using re-approved clinical drugs targeting the invasion and replication of SARS-CoV-2 cells. Repeated human ACE2 (APN01) was developed in 2010 and may reduce the virus and prevent serious lung damage. It has been shown to be safe and reduce the levels of angiotensin II and interleukin-6 in a phase II study of acute respiratory stress syndrome[92]. Investigations in China on complex COVID-19. A serine protease inhibitor camostat mesylate, approved in Japan for chronic pancreatitis and postoperative reflux

esophagitis, among other indications, has been shown to inhibit the activity of transmembrane protease serine 2 and to prevent the entry of SARS-CoV into cells.

This well-tolerated treatment has been proposed as treatment. inhibiting the activity of SARS-CoV-2 proteins, thereby preventing cell entry and infection control. Remdesivir is a comprehensive anti-viral agent that disrupts RNA duplication by acting as a nucleotide analog[93]. Originally designed to treat the Ebola virus, it has been shown to have an in vitro activity against SARS-CoV-2 and to prevent and reduce the severity of the disease in MERS coronavirus in primates. Clinical trials enroll patients in China and the United States[94]. Chloroquine (antimicrobial) and hydroxychloroquine (rheumatoid arthritis and treatment of systemic lupus erythematosus) inhibit SARS-CoV-2 in vitro cell invasion in the same focused areas treated with rheumatoid arthritis (500 mg twice daily with chloroquine and 600 mg twice daily followed by 400 to 600 mg / d of hydroxychloroquine) and trials with these agents are ongoing[94,95]. Preliminary studies suggest treatment to benefit from COVID-19 for weight loss of the severity of pneumonia, decreased length of hospital stay, and previous exposure to the virus[96].

The combination of the protease inhibitor lopinavir / ritonavir used to treat HIV infection has been shown to have in vitro activity against SARS-CoV and improved clinical outcomes when combined with SARS ribavirin. There have been reports of its success. in the treatment of SARS- CoV-2, although the first randomized, controlled trial did not show statistically significant benefit in patients with COVID-19[97]. Patients In this study of 199 patients, the 28-day regimen was 5.8% lower (95% CI, 17.3% to 5.7%) of patients treated with lopinavir / ritonavir and the median duration of improvement was shorter by 1 day. More information is needed to determine the role of lopinavir / ritonavir in the treatment of COVID-19. Antiviral drugs used for the flu (oseltamivir and arbidol) have been used, without the details of available clinical practice. Favipiravir, another drug approved for the common cold, is considered promising because it inhibits RNA polygamyase, and it is being studied in clinical trials in China[98].

Tocilizumab and sarilumab are interleukin-6 antagonists that are used in the treatment of rheumatoid arthritis, and tocilizumab also has the potential to treat cytokine release syndrome as evidenced by chimeric antigen receptor T-cell therapy. This may be a possible treatment option for patients with COVID-19 that exhibit cytokine or secondary hepopocytic lympho histiocytosis withinterleukin-6, ferritin, D-dimer and hs-cTnI. Tocilizumab has been successfully reported in patients with severe COVID-19 and clinical trials are underway. A recent sarilumab trial in the United States[99].

Management and Interventions

Currently, there are no approved treatments that have been shown to be safe and effective in COVID - 19, so the administration is very supportive. The aim is to diagnose the disease early, eliminate symptoms, and support organ function. Hospitalization may be required in extreme cases, and a clinical weakness scale may be used to assess whether admission to critical care is necessary. A common problem with COVID-19 is ARDS, so oxygen therapy is required in about 14% of cases. If patients do not respond to oxygen therapy, treatment may increase to continuous positive air pressure or positive air bi level pressure, intubation, mechanical cooling, or ECMO[100].

Due to the increasing global burden of the disease, several illegal therapies are used either as part of randomized or randomized controlled trials. The WHO launched the "Solidarity" trial on March 22, 2020 aims to find possible treatments to reduce the incidence of disease and reduce mortality rates[101].

Remdesivir, originally developed for the treatment of Ebola, has shown in vitro activity against SARS-Cov-2. Lopinavir and ritonavir are also commonly used antiretroviral drugs that have shown potential. there was a COVID-19 treatment. Anti-malaria, such as chloroquine and hydroxychloroquine are also being investigated for their potential prophylactic effects and treatment against COVID - 19[102].

Losartan, an angiotensin-II receptor antagonist is being investigated for its potential therapeutic benefits in COVID-19. As mentioned earlier, there are concerns about the safety of RAAS inhibitors in COVID due to studies reporting conflicting results. Therefore, Council on Hypertension European Society of Cardiology has issued a warning statement on starting or discontinuing ACEI and ARBs in the context of COVID - 19[103].

In addition, recovered plasma blood transfusions from patients diagnosed with COVID-19 showed promising results without any side effects. Immunoglobulin treatment of intravenous current. Further mention of more antibody cocktails for preventive and curative purposes[100]. A summary of these current and investigative therapies can be seen in[Table 3].

Table 3: A summary of current Mediations and treatments used currently under

Treatment	Stage
Supportive treatment:	
Noninvasive ventilation	Used in ARDS
Invasive ventilation	Used in ARDS if noninvasive ventilation fails
ECMO	Used in ARDS if noninvasive ventilation fails
Fluid resuscitation	Used to preserve organ function
Antiviral treatment:	

Remdesivir	In "Solidarity" clinical trial
Lopinavir	In "Solidarity" clinical trial
Ritonavir	In "Solidarity" clinical trial
Chloroquine	In "Solidarity" clinical trial
Hydroxychloroquine	In "Solidarity" clinical trial
RAAS inhibitors:	
Losartan	Being investigated—not yet in clinical trials
Immunomodulatory treatment:	
Convalescent plasma	In clinical trials
Intravenous immunoglobulin	Being trialed in small number of cases
Antibody treatment	In development

Abbreviations: ARDS, acute respiratory distress syndrome; ECMO, extra corporeal membrane oxygenation; RAAS, renin-angiotensin-aldosterone system.

Experimental COVID Drug use And Cardiovascular Adverse Effects

Numerous therapeutic agents have been used to treat patients with COVID-19, but a detailed review of this is beyond this review. We focus on the most promising drugs that have been reintroduced and used to treat the disease, emphasizing the negative effects of the CV of these treatments and known strategies to combat them. Among the therapies used are chloroquine and hydroxychloroquine, antiretrovirals (lopinavir and ritonavir), rivatarin, remdesivir, corticosteroids, anticytokine agents (IL-6 inhibitors), and therapeutic treatment. -immunoglobulin (convalescent plasma) has been prominent[104].

Chloroquine and hydroxychloroquine have been used to treat patients with COVID-19 in small clinical trials and have been shown to be effective in preventing cell proliferation through chronic trafficking and by exploiting the immune system by reducing cytokine. Both of these agents can cause an increase in QTc, as discussed earlier, which can be enhanced by the concomitant use of azithromycin, macrolide antibiotic, and other fluoroquinolones. Baseline electrocardiography is recommended for patients to evaluate long-term QTc in certain high-risk areas, as discussed earlier. Serial electrocardiography in critically ill patients following the development of these drugs is helpful in monitoring[105]. A detailed work flow of hydroxychloroquine treatment is given in. Lopinavir and ritonavir also have the potential to cause QTc expansion. Rivatirin has the potential to cause hemolytic anemia at high doses[106], which can also increase the risk of CVD and hemodynamic instability.

Future complications and implications

Without complications during the active phase of the infection, as described here, long-term follow-up of the disease remains possible despite the full consent of the virus. Previous epidemics from similar viruses may be useful in providing specific indications for long-term CV problems of COVID-19. For example, the 2002 SARS epidemic caused metabolic mutations with increased phosphatidylinositol and lyso phosphate dylinositol levels in returned SARS patients compared with healthy volunteers[107]. These metabolic changes have been associated with hyperlipidemia and dysfunctional glucose metabolism. Several studies have reported avascular necrosis as a chronic complication from corticosteroids given to SARS patients[108].

Anyway, the way it is leading to these physiological changes due to a viral infection remains unknown. Osteonecrosis is independently associated with an increased risk of adverse CV outcomes in SARS patients treated with corticosteroids and assays further testing. Mental illnesses, including chronic fatigue syndrome, have also been reported in patients recovering from SARS[109]. Given the strong association between mood disorders, such as depression and chronic fatigue syndrome, and CVD, such as chronic HF and cardiac arrhythmias, evidence supporting the long-term CV sequelae of these diseases appears compelling[110].

The outbreak of the epidemic has led to the conservation of medical resources, such as hospital beds, medical staff, and PPE, which has prioritized the care of COVID-19 patients. This has led to the fragmentation and reversal of selection processes, including structural processes and electrophysiology[111]. Recent studies have reported a decrease in cardiac catheterization / percutaneous intervention due to this modification of the management protocol[112], which has led to medication management as an alternative. Telemedicine and teleconsultations are widely used. As a result, there has been an unexpected increase in emergencies that occur while patients wait for their procedures. In addition, because of the fear of going to the hospital and receiving COVID, it seems that many patients are ignoring the important symptoms at home, which has led to many untimely deaths from the epidemic.

This is especially true with the STEMI episode, which has shown a dramatic decline during the epidemic, similar to the similar sharp increase in home mortality[113]. Clearly, such long-term consequences of our epidemic response must be mitigated in the future. Outbreaks appear to be exacerbated during the epidemic, with potentially increasing numbers of patients being turned away from non-compliance, delayed election procedures, and MI completed or presented late. Recent analyzes have shown a 38% decrease in primary PCI in the US during the COVID-19 epidemic, which is partly due to early hospital avoidance due to fear of infection in the hospital, STEMI misdiagnosis, and excessive use of fibrinolysis[112]. This could lead to an increase in the number of post-MI complications, such as mechanical problems, heart attacks, heart attacks, post-MI angina, and relapses, which were previously uncommon due to immediate treatment with an attack plan. Some of these problems may not have

been identified because of the deaths in the home. Similarly, a significant decrease in ACS hospital sleep levels in northern Italy has been noted[114]. Interestingly, the incidence of cardiac arrest outside the hospital has increased. Hiding symptoms such as shortness of breath, chest tightness, poor health status of patients with low to COVID, and fear of access to the health care system can be a factor in the increase in cases.

Future Directions

There is an urgent need for public health education; this is especially important for those with an existing CVD. A recent study from Hong Kong compared the introduction of ST - elevation myocardial infarction (STEMI) before and during the COVID-19 epidemic. It is reported that the time from symptom onset to early presentation was greater in patients with STEMI during the COVID-19 epidemic compared to years 2 in advance (318 vs 82minutes, respectively). Similarly, the injection department was also upgraded (129 vs 84.5 minutes)[115]. Overall, this suggests that patients with ACS are now more likely to present themselves later and the reasons for this are many. Patients may see hospitals as areas at high risk of COVID-19 transmission and, therefore, delay delivery. Other reasons may include the testing of COVID - 19, the availability of workers due to redistribution and the time taken for workers to wear protective clothing. Adjustments to established protocols and local guidelines are needed to help address the suspected ACS. In addition, clear communication is essential, so patients are reassured that hospitals are ready to deal with heart emergencies.

There are also potential long-term effects of COVID-19 on the cardiovascular system. A study involving 25 patients diagnosed with SARS 12 years after infection after infection found a difference in lipid and glucose metabolism compared to those without the virus[116]. It is too early to say what happens to COVID patients - 19, but it is necessary of follow-up as the clinical sequence of these metabolic disorders is well documented.

CONCLUSION

COVID-19, caused by SARS-CoV-2, is a real-time global epidemic. It is uncertain whether severe systolic heart failure is mediated by myocarditis, cytokine storm, microvascular dysfunction, minor thrombotic disorders, or alternative cardiomyopathy caused by stress. Many methods contribute to two different patterns of heart damage. Numerous symptoms of heart damage have been reported troponin has been proven to be a diagnostic and predictive tool. As the new epidemic continues to unravel, a variety of hearts are at stake. There is a need for further research to better understand the scope of CV references. Until a vaccine or treatment is available, doctors should be aware of the known cardiac involvement and deal with this initially to reduce the risk. Cardiac comorbidities are common in patients with COVID-19 and these patients are at high risk of illness and death. Many promising treatments are still being investigated, but none have been clinically effective so far.

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