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Systematic Study Of Covid-19 And Cardiac Arrhythmic Disease

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Abstract: Coronaviruses, an enveloped RNA virus family, can infect many animals, including humans. Pathogenicity of human coronaviruses SARS, MERS, and SARS-CoV2 are among the most dangerous. Initial bat-to-human transmission is likely cross-species. The first transmission was in Wuhan and examined COVID-19 victim assessment and counseling. However, it emphasizes the interprofessional team's role in evaluating and treating cardiac problems.

Keywords: Covid 19, Cardiovascular, Patient care, epidemiology

Study Objectives:

- ***Review COVID-19 epidemiology.***
- ***Describe the COVID-19 patient's symptoms.***
- ***Describe the COVID-19 patient's therapy options.***
- ***A patient with COVID-19 cardiac symptoms has a prognosis.***

1. INTRODUCTION

From 32 to 46 percent of COVID-19-infected patients in China had underlying medical disorders such as hypertension (15 to 31 percent), cardiovascular disease (14.5 to 15 percent), and diabetes (10 to 15%). (10 percent - 20 percent)., The presence of hypertension, cardiovascular disease, and diabetes was found in 17.1% of COVID-19 trials[1-3]. The prevalence of cardiovascular disease ranged from 40% to 60% in a study of 99 COVID-19 participants. In large studies of over 1000 COVID-19 individuals, 4% to 2% exhibited abnormalities[4-5].

Acute cardiac damage, cardiomyopathy, and heart failure are linked to COVID-19 mortality. The mortality rate of COVID-19 patients with coronary heart disease was 10.5 percent higher than the overall mortality rate. Coronary heart disease and myocardial injury have the greatest fatality rate[6].

SARS-CoV-2 penetrates host cells via AChE2 (ACE2). Both pharmacological RAS inhibitors and RAS-related disease elevate ACE2, facilitating SARS-CoV-2 entrance into the lungs and heart. As a result, the infection may directly influence CVD (Fig.1). ARDS and pneumonia are among the more dangerous conditions[7-9]. Some patients' hearts can be harmed regardless of previous cardiovascular diagnoses. Increased troponin levels in COVID-19 patients could be due to stress cardiomyopathy, hypoxia, cardiac microvascular damage, epicardial coronary artery disease, or systemic inflammation response syndrome (cytokine storm)[10-12]. A high troponin level may be associated with symptoms and signs of an acute

coronary syndrome in a minority of patients. To prevent the spread of SARS-CoV-2 in the workplace, early identification and isolation of patients with suspected SARS-CoV-2, proper PPE, hand hygiene, and environmental disinfection are recommended[13].

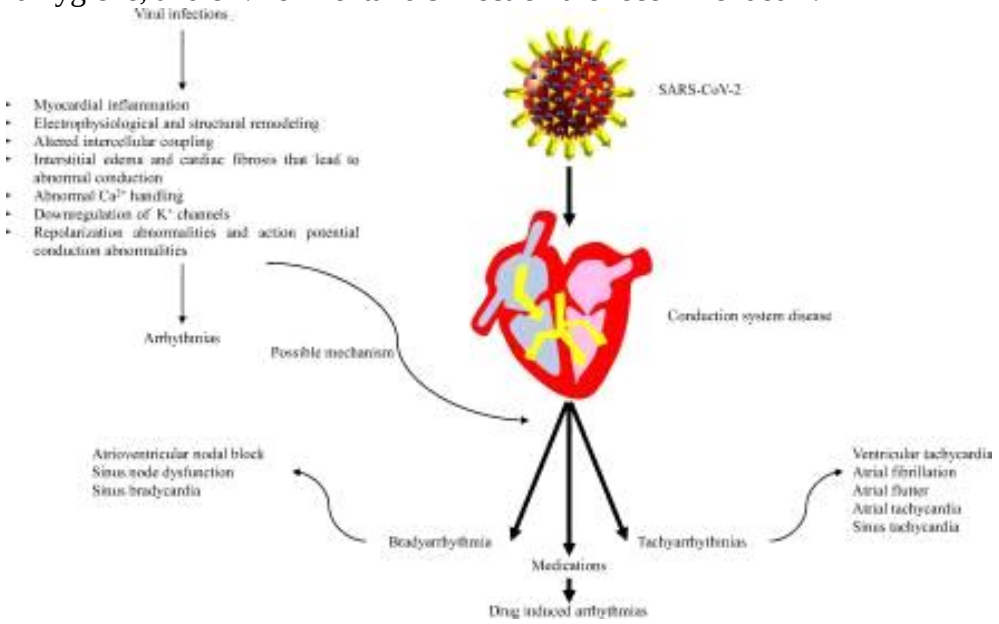

Fig 1: Possible mechanism of cardiac arrest in pandemic

SARS CoV-2 late life

SARS-CoV-2 genomic RNA encodes ORF1a and ORF1b polypeptides. The viral nsp3 and nsp5 viral proteases convert the polypeptide chains into 15-16 nsp units. Most nsps in the viral replication and transcription complex are involved in viral replication and transcription[14-16]. The spike, nucleocapsid, membrane, and envelope proteins are assembled in an endoplasmic reticulum-Golgi intermediate compartment[17].

Involvement of cardiac in viral disease

Viral myocarditis affects the sinoatrial (SA) and atrioventricular (AV) nodes. Myocarditis begins with virus infection, entry, and growth in the myocardium. Phase two (the autoimmune phase) involves activating T cells, cytokine production, and cross-reacting antibodies. To generate antibodies, the heart undergoes remodeling and dilatation (phase three). Acute viral myocarditis and pericarditis commonly resolve without symptoms. However, viral myocarditis often causes ventricular arrhythmias. Case studies relate arrhythmias to viruses like influenza, Epstein-Barr, and HIV. Sardana et al. investigated nearly 17 million HIV-positive adults. They found that even after adjusting for race, age, gender, socio-economic status, and obesity, patients with HIV had a 1.46 hazard ratio for developing atrial fibrillation[18-20]. A 45-year-old man with transitory non-sustained ventricular tachycardia had flu virus-focused myositis with conduction tissue inflammation, according to Andrea Frustaci and colleagues. The H1N1 influenza virus caused respiratory failure in an 18-year-old lady who had a high-degree atrioventricular (AV) block after the virus caused respiratory failure[21]. Abdalla et al. discovered atrial fibrillation in a Zika patient. Less than half of the Zika patients developed atrial fibrillation. These cytokines can cause inflammation and arrhythmias. An immunocompetent patient with acute EBV infection and myocarditis who went into cardiac arrest and had a malignant ventricular arrhythmia has been reported.

According to this study, despite its common mildness, viral myocarditis is hazardous and potentially fatal. In a study, 75 patients with acute respiratory infections and/or viral illnesses (influenza, parainfluenza, and adenovirus) were followed for 3 to 26 years (mean, 14.6 years). They observed that 42.3% of patients had recurring and complicated ventricular extrasystole on resting electrocardiogram (ECG) for years, and 89.3% had fibrous pericardial lesions, indicating pericardial involvement22-24. SARS-CoV-2, which induces COVID-19, can harm heart muscle. It is due to a few things. The coronavirus penetrates cells when it binds to ACE-2 receptors in the heart. Inflammation in the circulation can affect the heart. The immune system's fight against the virus may cause damage to healthy tissues like the heart. A coronavirus infection can cause inflammation, damage to tiny capillaries, and blood clots, decreasing blood flow to the heart and other essential organs. Severe COVID-19 affects endothelial cells that line blood vessels.

Cardio-vascular and Covid-19

CVD often occurs in SARS and MERS patients. Several investigations on COVID-19 patients' clinical features have revealed similar findings. Cardiovascular disease and associated risk factors, such as hypertension and diabetes mellitus, were common among COVID-19 patients, but the classifications used in each study varied[24]. In Wuhan, China, on January 2, 2020, 41 COVID-19 patients hospitalized had a comorbidity prevalence of 32%. Diabetes (20%), hypertension (15%), and other cardiovascular illnesses (15 percent). Later studies found these comorbidities to be common. These pre-existing illnesses were much more common in highly unwell people (like ICU patients) or died[25-26]. A cohort study in Wuhan, China, indicated that 46% of 138 COVID-19-infected people had comorbidities, with 31% having hypertension and 15% having other cardiovascular disorders. 10% had diabetes (22 percent of patients in the ICU). According to a multicenter cohort study in Wuhan, 48% of individuals evaluated had any comorbidity (65% died), 30% had hypertension (45% died), 19% were diabetic, and 8% had coronary heart disease (24 percent of those who died). A study of 1,099 COVID-19-infected mainland Chinese people found that 24% had hypertension, 24% had diabetes, and 3% had coronary heart disease (3 percent) 6% of seriously unwell patients[27].

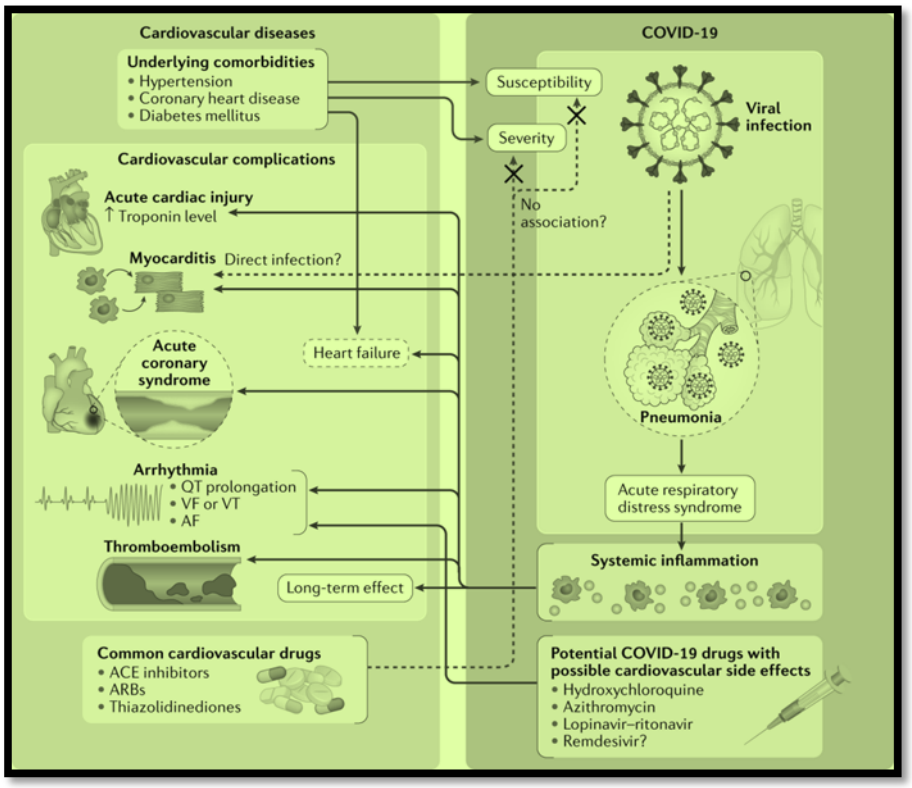

Fig: 2 interaction between Cardiovascular and Covid-19 Pathophysiology

ACE2 Receptor

SARS-CoV-2 penetrates cells by interacting with ACE2 receptors. Endothelial cells, for example, express the ACE2 receptors seen in both types of pneumocytes. ACE2 controls the renin-angiotensin-aldosterone cycle. SARS-CoV-2, like other coronaviruses, targets the respiratory system using ACE2 receptors[28].

SARS-CoV-2 and the Immune Response

The immune response to COVID-19 involves two steps. At this stage, adaptive immune systems are trying to kill the virus. However, if there are any flaws, SARS-CoV-2 will spread and cause systemic organ damage, with the lung, endothelium cells, heart, and kidneys being particularly vulnerable. Second, significant injury causes acute inflammation in the injured organs[29]. Diabetes, atherosclerosis, and obesity have been demonstrated to suppress the immune system. These were connected to poor prognosis in COVID-19.

COVID-19 Cardiac Damage Mechanisms

Multiple mechanisms for cardiac damage have been hypothesized based on previous SARS and MERS outbreaks and the ongoing COVID-19 epidemic. Large amounts of cytokines released in severe COVID-19 can harm several organs, including the vascular endothelium and cardiac myocytes—the systemic inflammatory reaction[30].

Cytokine Release Syndrome

Infection with COVID-19 produces cytokine release syndrome. Proinflammatory cytokines such as IL-2, IL-10, IL-6, IL-8, and TNF- are significantly increased in severe cases. Cytokines can cause ARDS and other end-organ damage during the virus infection (phase 1) and the ongoing severe inflammation (phase 2)[31].

Direct Myocardial Cell Injury
An altered ACE2 pathway causes immediate lung, cardiac, and endothelial cell injury. SARS-CoV2 has been linked to viral myocarditis in a few cases. In most cases, however, myocardial damage was caused by increased cardiometabolic demand from systemic infection and hypoxia from severe pneumonia and ARDS.

Coronary Acute Syndrome
The acute coronary syndrome can occur due to systemic inflammation and increased catecholamines. Acute coronary syndrome is likely caused by coronary thrombosis in COVID-19 patients[32].

Other Possible Mechanisms
Cardiotoxicity can occur from corticosteroids, antiviral medications, or immunotherapy. Electrolyte imbalances, which can occur in any acute systemic illness, can cause arrhythmias in patients with underlying heart disease. The SARS-CoV-2 interaction with the renin-angiotensin-aldosterone pathway puts COVID-19 patients at risk for hypokalemia. Hypokalemia has been associated with certain arrhythmias[33].

Treatment and Management of Covid 19 and cardiovascular disease

COVID-19 Patients Get Total Cardiovascular Care
Early detection and therapy of cardiac illnesses and adequate protection against COVID-19 exposure must be prioritized for COVID-19 patients' cardiac care needs. A clear message should be sent to individuals with cardiac warning symptoms, have correctly said. Masks and physical separation are still needed. COVID-19-related cardiovascular illness is being studied by clinicians and researchers at the same time[34-36].

ACE inhibitors (ACEI)/ Angiotensin Receptor Blockers (ARB)
By early 2020, concerns regarding these drugs' safety in COVID-19 patients arose. The current consensus is to use these medications as long as possible. Those on continuous ACEI/ARB and hospitalized for COVID-19 had no significant difference in days alive and out of hospital compared to those on intermittent ACEI/ARB. COVID-19 patients can utilize five of the most commonly prescribed antihypertensive classes without raising their infection risk[37].

Remdesivir
Remdesivir is an RNA polymerase inhibitor for COVID-19 (antiviral). A double-blind, multicenter RCT on adult patients with severe COVID-19 was undertaken in China. In terms of clinical improvement, there was no difference between the treatment and control groups. The US National Institute of Allergy and Infectious Diseases funded a remdesivir therapy trial with over 1,000 COVID-19 patients. Patients who received remdesivir healed faster than those who received a placebo. The FDA has approved remdesivir for use in all COVID-19 infected Americans. As the COVID-19 pandemic progresses, remdesivir's cardiovascular side effects may change[38-39].

Hydroxychloroquine and Chloroquine

A single-group open-label study in France suggested hydroxychloroquine as a COVID-19 treatment. However, an observational study of COVID-19 patients hospitalized in New York found no evident benefit from hydroxychloroquine. Using all three therapies alone or with azithromycin did not affect the composite outcome of intubation or death. Atrioventricular block and QTc prolongation have been associated with chloroquine and azithromycin. The FDA discontinued hydroxychloroquine and chloroquine emergency use permission for COVID-19 patients due to lack of therapeutic effectiveness and potential cardiovascular side effects[40-41].

Azithromycin

Early in the pandemic, azithromycin and hydroxychloroquine were frequently used in conjunction as a therapy. Some clinical trials have failed to show any clinical advantage from this combination. As a macrolide, azithromycin is known to harm the QTc interval. An increased risk of torsade de pointes and QTc prolongation are possible side effects of azithromycin and chloroquine or hydroxychloroquine combination therapy. COVID-19 azithromycin use has been discouraged by the clinical ineffectiveness and risk of cardiac arrhythmias[42].

Lopinavir-ritonavir

Protease inhibitors for HIV-1 include lopinavir and ritonavir. Researchers from the New England Journal of Medicine reported no benefit from lopinavir-ritonavir treatment for severe COVID-19. It should be taken with caution in people with the cardiovascular disease since it may interact with antiarrhythmics, antiplatelets, and anticoagulants metabolized by cytochrome P-450 3A4.

Steroids

The WHO recommends using systemic steroids to treat COVID-19 infection. Inflammatory effects of corticosteroids have led to extensive research in treating sepsis and ARDS. In addition to fluid retention, these medicines can cause electrolyte imbalance, hyperglycemia, and hypertension. Concerns about COVID-19's steroids were raised during the SARS-CoV outbreak that preceded this one. It was investigated in the recent RECOVERY research in COVID-19 patients on invasive mechanical ventilation or oxygen. Dexamethasone saved one-third of those on mechanical ventilation and one-fifth on oxygen treatment[43-44].

Aspirin

A retrospective study related low-dose Aspirin to better results in COVID-19 patients.

Tocilizumab

Tocilizumab, an IL-6 receptor antibody, is being researched for COVID-19 patients in hospitals. Those with COVID-19 had greater levels of IL-6 and those with more severe illness. Tocilizumab's anti-inflammatory properties can help treat diseases, including ARDS and mortality. Tocilizumab has been demonstrated to elevate cholesterol levels. However, the long-term effects on cardiac morbidity and mortality remain unknown[45].

Plasma of Convalescent

Convalescent plasma is harvested from patients who have recovered from COVID-19 and built an immunological response. A few case reports and randomized trials have shown that

convalescent plasma can aid hospitalized COVID-19 patients, especially if given early in the illness[46]. The FDA has cleared the use of convalescent plasma in COVID-19 patients hospitalized.

Ivermectin

Ivermectin may help COVID-19 patients. Ivermectin is used to treat Strongyloides and onchocerciasis. Dr. Andrew Hill analyzed 18 randomized clinical trials that used Ivermectin. In six randomized trials, moderate or severe infection reduced mortality by 75%. In another randomized trial of 476 individuals, Ivermectin did not affect shortening sickness duration. Four people had multiple organ failures. The FDA strongly advises against using Ivermectin to prevent or treat COVID-19 infection (FDA).

Vaccination

Researchers have been working on a vaccine since the SARS-CoV-2 genetic sequence was published in January 2020. Around 90 vaccines are now in development. Many countries have already started. The FDA has approved Pfizer and Moderna's mRNA-based vaccinations for emergency use (FDA). Previously, these vaccinations were given to many healthcare staff. ChAdOx1nCov-19 caused immunothrombotic thrombocytopenia[47]. A few times, a vaccine had an unfavorable effect. Heparin-induced thrombocytopenia works similarly.

Acute Cardiovascular Complications of Covid-19 Diagnosed

Early identification of COVID-19 is critical. COVID-19 can cause chest tightness and heart palpitations despite being a respiratory infection. A cardiovascular evaluation should be performed on all patients with risk factors or pre-existing CVD, cardiovascular symptoms or ECG abnormalities, elevated cardiac biomarkers, or hospitalization. Because SARS-CoV-2 is highly contagious, limiting diagnostic modalities to those directly affecting patient treatment. Telemetry should be used for all in-hospital cardiovascular assessments but is vital for critically ill patients[48].

A baseline ECG should be obtained at admission and repeated daily in patients with severe COVID-19 infection to detect new arrhythmias. The usage of hydroxychloroquine and azithromycin should be monitored for QTc prolongation. On average, individuals receiving chloroquine/HCQ plus azithromycin had a QTc 500 ms, compared to 453.3 ms in the monotherapy group. Heart troponin and NT-proBNP levels should be evaluated upon admission, and if elevated, patients should be closely monitored. Patients with high troponin levels in COVID-19 are more likely to die in hospitals. If a POCUS ultrasonography shows aberrant results, a TTE should be avoided. Echocardiography and vascular ultrasonography should be used in severe COVID-19. On cardiac ultrasonography, patients with L-type dyspnea COVID-19 may have higher respiratory effort, diastolic ventricular septal shift, left ventricular hypo-diastole, and decreased stroke volume[49].

However, cardiac ultrasonography may reveal myocardial injury in patients with high pulmonary elastance receiving positive-pressure mechanical ventilation. A cohort analysis of 100 recently recovered COVID-19 patients revealed that 78% had cardiac involvement and 60% had chronic myocardial inflammation. Coagulation marker monitoring is required in COVID-19 patients with D-dimer concentrations above 1 ng/ml. Combining vascular ultrasound and compression ultrasonography can identify DVT in mechanically ventilated patients. The NLR and PLR can be used to predict COVID-19 illness severity (PLR). NLR was found to be a superior predictor of progression from mild to severe disease with an

optimal threshold of 3.3 and the highest AUC (AUC). Of 222 COVID-19 patients, those with high NLR and IgG levels had the most severe illness (72.3 percent; 34/47). Mechanical breathing was the most common among patients with high NLR and IgG levels (44.1%) but had the lowest recovery rates (58.8%; 20/34). A meta-analysis related greater WBC, neutrophil, prothrombin time, D-dimer fibrinogen, ESR, IL-6, and IL-10 levels to severe disease, ICU admission, and poor outcomes in COVID-19 patients[50].

Non serve cases	**Severe cases**
Telemetry	-
ECG (on admission)	ECG (daily)
Cardiac biomarkers: Troponin, NT- proBNP	Cardiac biomarkers: Troponin, NT- proBNP (Daily)
Inflammatory Maker: CRP, Ferritin, PT, PTT	Inflammatory Maker: CRP, Ferritin, PT, PTT (daily)
Coagulation marker: D-dimer, Fibrinogen, PT, PTT	Coagulation marker: D-dimer, Fibrinogen, PT, PTT Daily)
-	Formal TTE and Cardiology Consult if POCUS and 12 lead ECG abnormal.

Table: 1 Diagnosis complication of cardiovascular

2. CONCLUSION

In COVID-19 patients, the emergence of new CMPs or the aggravation of existing CMPs is common. In these patients, they also increase mortality and morbidity. COVID-19 CMPs cause multiorgan failure, ARDS, and cardiogenic shock in patients. Thus, COVID-19 diagnostic measures should include cardiovascular comorbidities. Early in the course of this unique disease, history, signs, and symptoms of cardiac injury should be considered, and quick therapeutic actions to prevent exacerbating cardiac status should be explored[51]. COVID-19 patients with cardiovascular issues make up the majority of ICU admissions, needing intubation, mechanical ventilation, and eventually dying. Pre-existing CVD patients must be risk-stratified before admission. Moreover, all COVID-19 management team physicians must be aware of the cardiovascular implications of COVID-19 to quickly detect and manage the clinicopathological symptoms, which may help anticipate disease severity and enhance COVID-19 patient survival rates. A cardiologist should also be part of the COVID-19 care team to guide efficient treatment methods.

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