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Potential Cardiac Tamponade Development Secondary to SARS-CoV-2 Infection

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Abstract: Upon initial discovery in late 2019, severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, has managed to spread across the planet. A plethora of symptoms affecting multiple organ systems have been described, with the most common being nonspecific upper respiratory symptoms: cough, dyspnea, and wheezing. However, the cardiovascular system is also at risk following COVID-19 infection. Numerous cardiovascular complications have been reported by physicians globally, in particular cardiac tamponade. Physicians must hold a high index of suspicion in identifying and treating patients with cardiac tamponade who may have contracted the novel coronavirus. This review will describe the current epidemiology and pathophysiology of SARS-CoV-2 and cardiac tamponade, highlighting their clinical course progression and the implications it may have for the severity of both illnesses. The paper will also review published case reports of cardiac tamponade, clinical presentation, and treatment of this complication, as well as the disease as a whole. (Curr Probl Cardiol 2023;48:101417.)

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The novel SARS-CoV-2 virus emerged in Wuhan, Hubei province, China, as a new, easily transmissible pathogen leading to severe acute upper respiratory symptoms. SARS-CoV-2 has quickly spread globally, leading to a current international pandemic. This global tragedy has lasted for the better part of the last 18 months and is still yet to have been controlled. As of October 12, 2021, there have been 238,557,111 cases reported globally, and of that 862,317 people have succumbed to the virus, according to Johns Hopkins University Coronavirus resource center. The United States of America has accounted for 44,515,976 of those cases and 715,078 of those deaths. The World Health Organization has termed the disease "COVID-19." The average duration of incubation is approximately 5 days long and the main symptoms exhibited in those affected by COVID-19 are like those most commonly observed in patients with pneumonia: fever, cough, fatigue, headache, and myalgia.

While the comprehensive pathophysiology of the virus is still being researched, what is known is that the virus causes diffuse alveolar damage, which reduces oxygen saturation in the alveoli. Critically ill patients can also suffer from a cytokine storm response by the body in an attempt to eliminate the virus. The release of cytokines leads to indirect damage to the myocardium and pericardium via the cytokine storm.

COVID-19 induced myocarditis and pericarditis may also result in the development of cardiac tamponade. The virus uses the ACE2 receptor, Angiotensin-Converting Enzyme 2, to enter and invade cells. ACE 2 is commonly found in type 2 alveolar cells, leading to the high incidence of primary pulmonary manifestations. COVID-19 has also shown the use of ACE2 receptors to invade cardiomyocytes; however, it is still unclear whether this is the primary mode of infection. Many patients who developed cardiac tamponade may also have other underlying cardiac manifestations, such as biventricular heart failure and cardiac arrest. ACE2 receptor expression is often upregulated in heart failure patients, which may serve further to potentiate not only cardiac but also systemic inflammatory damage. The findings reported throughout this literature review help to provide education on cardiac tamponade as a potentially life-threatening complication secondary to COVID-19 infection. The aim is to provide physicians and healthcare providers with a better understanding of cardiac tamponade in order to identify and treat this complication in COVID-19 infected patients as rapidly as possible. This review will
introduce the current epidemiology of COVID-19 both globally and domestically, present the pathophysiology of COVID-19, particularly in the development of cardiac tamponade, report on documented cases of cardiac tamponade, and summarize the therapeutic options available to those infected patients who develop cardiac tamponade.

**Methods**

The following search was conducted in October 2021 through the PubMed database to determine the cardiovascular complications manifested in COVID-19 positive patients. The first search was through all fields containing search words such as "COVID-19," "cardiovascular," "symptoms," “SARS-CoV-2,” "Cardiology." This search exhibited the basis for potential cardiovascular symptoms that have been documented due to COVID-19 disease. Our initial investigation highlighted the increase in the incidence of various cardiovascular complications seen among positive patients, ranging from hypertension to congestive heart failure. In particular, we noted patients were presenting with rare cardiac tamponade as a result of COVID-19 infection. A secondary round of searches was done through the PubMed database, using keywords such as "COVID-19," "cardiac tamponade," "myocarditis," and "cardiovascular disease." The initial search phrase “Covid-19 Cardiac Tamponade” yielded 64 pieces of literature with the aforementioned keywords. We picked cases in which cardiac tamponade occurred secondary to COVID-19 infection. Cases of post COVID-19 vaccination leading to cardiac tamponade development were excluded as we sought only articles of primary infection. However, further research should be conducted into the COVID vaccine and the development of cardiac tamponade if any relationship may exist. Furthermore, only cases of adult cardiac tamponade were chosen as ages (18+) were our core demographic. We also strayed away from cases in which other pathology developed, only including cardiac tamponade as the primary manifestation, and excluding others. Following our exclusion criteria, we were left with 7 articles containing 9 case reports of patients who developed cardiac tamponade following COVID-19 infection. We have compiled multiple case reports, literature reviews, and meta-analyses to present the epidemiology, transmission, and incidence of COVID-19 in relation to cardiac tamponade. Due to the recent nature of SARS-CoV-2, all articles published from 2020-present were considered as no prior literature had existed. Further research into the risk factors and transmission of COVID-19 is ongoing and should continue to be conducted as an increasing number of patients may present
with atypical cardiovascular symptoms, including but not limited to pericardial effusion and cardiac tamponade.

**SARS CoV-2 Epidemiology**

Cases of COVID-19 have been reported all across the globe as all age groups seem to be affected in some capacity. However, elderly patients seem to be more adversely affected. The most common clinical phenotypes of COVID-19 include muscular soreness, fever, dyspnea, and cough, while some atypical symptoms include both vomiting and diarrhea. The clinical signs and symptoms vary with the extent of the disease in each patient. The severity of COVID-19 infection has ranged from asymptomatic to critically ill patients. Asymptomatic infection can be defined as patients who have a positive PCR test for SARS-CoV-2 infection yet present with no clinical signs or symptoms of infection. Severe infection is defined as oxygen saturation below 92% with dyspnea that rapidly progresses, and acute infection as patients with respiratory failure, shock, or multiple organ system failures. Regarding severe and acute COVID-19 patients, a systematic review and meta-analysis of 6007 articles and 212 studies found that diabetes, malignancy, and underlying immunosuppression were all strongly associated with severe COVID-19 infection.

Various risk factors for COVID-19 infection exist, which vary from demographics, comorbidities, and lifestyle. Being of older age and the male gender has been associated with higher COVID-19 disease severity. Patients who were male and older spent significantly more time on ventilation and required intensive care. In addition, a study analyzing 10,926 COVID-19 related deaths concluded that black and south Asian patients were found to have a higher mortality risk compared to white patient subjects. A literature review of risk factors associated with COVID-19 concluded that it disproportionately affected black and other minority races with increased risk of hospitalization, severity, and mortality to COVID-19. Arterial hypertension was more frequently seen in patients with severe COVID-19 than without it, though it should be taken into consideration that hypertension is more common in elderly patients. Diabetes and obesity are other well-known risk factors for severe disease or death from COVID-19. A meta-analysis showed that COVID-19 patients with diabetes had a higher risk of severe disease, death, and a higher rate of I.C.U. admissions.

As COVID-19 continues to spread across the globe, the demand for vaccinated individuals grows increasingly more important. As more and
more people are infected, many different symptoms and outcomes are documented and reported. Numerous pulmonary and extrapulmonary manifestations of COVID-19 have been noted to date. More and more patients complain of or have been diagnosed with cardiovascular complications secondary to COVID-19. In a study of 416 COVID-19 positive patients, some form of cardiac injury was detected in 19.7% of the group.\(^\text{13}\) This high prevalence of cardiac injury has also been associated with increased mortality. Further, another study posited that 27.8% of their 187-patient population had developed myocardial injury secondary to COVID-19.\(^\text{14}\) Cardiovascular complications can include, but are not limited to, tachycardia, hypertension, myocarditis, and left ventricular dysfunction.\(^\text{13}\) Although complete statistics on the exact number of patients who developed cardiac tamponade is not available; there have been at least 7 cases reported on and are available through the PubMed database.

**SARS-CoV-2 Pathophysiology**

SARS-CoV-2 is a member of the *Coronaviridae* family, a family of large, enveloped, positive-sense, single-stranded R.N.A. viruses. Specifically, SARS-CoV-2 belongs to the Betacoronavirus genus and the Orthocoronaviridae subfamily.\(^\text{15}\) The virus shares a similar genome to previous coronaviruses: MERS-CoV (middle eastern respiratory syndrome coronavirus) and SARS-CoV-1 (sudden acute respiratory syndrome coronavirus 1). The anthropophilic transmission of respiratory droplets ejected from the nasopharynx primarily spreads COVID-19. Following direct contact with an infected individual and inhalation of respiratory droplets, the virus can enter the upper respiratory tract, in which it invades cells and replicates.

The virus uses the receptor Angiotensin-Converting Enzyme 2 or "ACE2" to enter and invade cells.\(^\text{13-15}\) Spike (S) glycoproteins on the virus specifically attach to ACE2, which are then activated using transmembrane serine protease 2, “TMPRSS2,” which leads to entrance into the cell.\(^\text{15}\) Upon entering the cell, the viral coat is removed, allowing the genome to be transcribed and translated, leading to the multiplication of the virus. ACE2 or Angiotensin-converting enzyme 2 is found primarily in the lungs’ type II alveolar pneumocytes, leading to the predominance of symptomatic pulmonary manifestations. ACE2 becomes downregulated after COVID-19 infection leading to the production of reactive oxygen species, “R.O.S.,” further potentiating alveoli and lung damage.\(^\text{15}\)
Following the entry of the SARS-CoV-2 virus into cells, a plethora of pro-inflammatory cytokines are produced, further potentiating damage to the tissue in the organ of infection. Interleukin 6 (IL-6) is generated by those affected leukocytes around the area of infection. Further inflammatory markers: IL-1β, IL-8, IL-12, tumor necrosis factor α (TNF-α), interferon-gamma inducible protein 10 (IP10), macrophage inflammatory protein 1A (MIP1A), monocyte chemoattractant protein 1 (MCP1), and interferon-gamma inducible protein (IP10) are also increased in COVID-19 infected patients. Increased amounts of these proinflammatory cytokines may be another factor causing injury to cardiac myocytes. However, it is still not known whether injury occurs due to direct viral damage, systemic inflammation, or a combination of both factors.

In a study conducted by Xin Zhou et al., it was concluded that greater than 7.5% of cardiac myocyte expressed ACE-2 receptors, postulating that the heart has an increased risk of being affected by COVID-19. This risk is further increased in cases of COVID-19 being present in blood, otherwise known as viremia. Magadum et al. describe numerous cardiovascular manifestations of COVID-19, and postulates that the virus can indeed infect cardiac myocytes, which can lead to cytotoxic effects. Studies have shown that SARS-CoV-2 can be isolated from cardiac myocytes using RT-PCR, thus further supporting the theory of the virus’s ability to cause direct injury to cardiac myocytes. This proves to be especially alarming, as the virus’s ability to injure cardiac muscle may lead to significant cardiovascular as well as systemic issues. Damage to cardiac myocytes may lead to a significant increase in both morbidity and mortality in those COVID-19 positive individuals. Guo et al. also noted that patients with heart failure express more ACE2 receptors on cardiac myocytes and are thus more susceptible to increased cardiovascular manifestations due to SARS-CoV-2.

Due to the novelty of the SARS-CoV-2 pathogen, it has been difficult to determine the exact specific clinical manifestation the virus causes. The emerging disease has many complexities, of which new information is being gathered with every passing day. A report on a 59-year-old male patient who, on February 16, 2020, underwent coronary artery bypass surgery due to non-ST elevation acute coronary syndrome was reported. Upon extubation it was discovered he had mild pericardial effusion of insignificance and was released from the hospital. This patient tested positive for COVID-19 on March 5, 2020, during the early days of the pandemic. As he underwent a treatment regimen of antibiotics and antivirals, he also underwent pericardial fluid drainage, which was sent to a lab for cytological and chemical analysis. A rRT-PCR amplification of SARS-
CoV-2 RNA through GeneFinder COVID-19 PLUS RealAmp Kit was used to detect 3 SARS-CoV-2 targets: the envelope protein (E), the nucleocapsid protein (N), and RNA-dependent RNA polymerase (RdRp) genes. RT-PCR of the pericardial fluid revealed the presence of the SARS-CoV-2 N gene. Due to only 1 of the 3 genes being localized in the sample suggests that while still present, the viral load may be low. The specimen quality was confirmed with nasopharyngeal swabs, thus confirming the accuracy of the fluid analysis. The presence of SARS-CoV-2 in pericardial fluid may serve as yet another clue as to how COVID-19 pathophysiology may affect the cardiovascular system and potentially lead to life threatening pericardial effusion and cardiac tamponade.

**Cardiac Tamponade**

Cardiac tamponade is defined as an abnormal amount of fluid accumulating in the pericardial sac surrounding the heart. Cardiac tamponade is a relatively rare yet deadly condition which can occur due to a number of both acute and chronic pathologies. There are around 2 cases per 10000 people in the United States alone, with males being affected more often than females. While the total number of COVID-19 patients who developed cardiac tamponade is unknown, numerous cases have been reported, with more being reported as the pandemic continues. The pericardial sac can store varying amounts of fluid leading to different maximum volume tolerated in different patients. Fluid accumulation of as little as 200 ml to upwards of 2L may lead to cardiac tamponade development.

Pericardial effusion, in turn, leads to compression of the heart musculature, which causes systemic shock due to a decrease in cardiac output. There are numerous etiologies that cause cardiac tamponade with the most common being rupture of the ventricles from either a myocardial infarction or a prior penetrating wound. These etiologies lead to a rapid increase in fluid in the pericardial sac which is much more emergent than slow accumulations of fluid. Slow accumulations of pericardial fluid are more often caused by systemic rather than acute injuries and illnesses and are thus better tolerated by the pericardium. Most often, some form of neoplasm or autoimmune disease contribute toward the slow increase in pericardial fluid volume. Cardiac tamponade is considered a medical emergency and should be identified and treated swiftly as cardiac arrest can quickly onset.

A decrease in cardiac output occurs due to decreased diastolic filling when the left ventricle becomes compressed by the excess pericardial fluid surrounding the heart myocardium. Further, central venous pressure
also increases as there is compression of the right atrium, leading to impaired venous return. This can eventually lead to right ventricular collapse. Patients may present with a variety of signs and symptoms, with the most common initial symptom being tachycardia. Dyspnea, cough, weakness, and lightheadedness are additional reported symptoms of note. The heart rate begins to rapidly increase in order to compensate for the current loss in cardiac output. Pulsus paradoxus is usually present, showing pericardial effusion is causing cardiac tamponade. Upon performing a physical exam, Beck’s triad of muffled heart sounds, hypotension, and jugular venous distension are 3 findings routinely seen in patients suffering from cardiac tamponade. To further confirm the diagnosis of cardiac tamponade electrocardiogram, ECG, or echocardiography may be utilized. The classic ECG finding of electrical alternans, alteration of the QRS amplitude, is frequently seen. The echocardiogram aids in localizing the size and amount of the pericardial effusion, causing the cardiac tamponade. History, physical exam, and confirmatory tests should all be used holistically in order to confirm the diagnosis of cardiac tamponade.

Reported Cases of Cardiac Tamponade in SARS-CoV-2 Positive Patients

Case 1: Cardiac tamponade in COVID–19 patients: Management and outcomes

Patient 1: A 48-year-old Hispanic male with a past medical history of type 2 diabetes mellitus, morbid obesity, and a known chronic small pericardial effusion of unknown etiology and presented with dyspnea and acute deterioration for the past 24 hours. A nasopharyngeal swab was positive for COVID-19. Following a comprehensive workup, the most notable findings included a large cardiac silhouette on chest x-ray (CXR), and a moderate-to-large pericardial effusion with tamponade physiology on Echocardiogram (ECHO). Treatment included emergent percutaneous drainage of pericardial fluid and initiation of therapeutic anticoagulation. On postoperative day 8, the patient developed acute cardiovascular decompensation, with signs of obstructive shock and a large pericardial fluid collection on ECHO. Patient underwent another pericardial drainage and was then switched to prophylactic dose anticoagulation. After a drop in the inflammatory markers and a return to stable conditions, the patient was discharged.
Patient 2: A 56-year-old Hispanic male with no significant medical history other than a BMI of 27.1 presented with a 1-week history of chest pain, fever, chills, and cough. Lab results showed elevated serum troponin levels and a confirmed COVID-19 swab. Patient developed progressive hypotension over the course of a few hours and an emergent bedside ECHO displayed a large pericardial effusion with tamponade physiology. Additionally, the patient also had a left ventricular ejection fraction of 20%. Upon emergent drainage, the patient developed cardio-pulmonary arrest and expired. It can be assumed that the cause of death was cardiogenic shock due to severe ventricular dysfunction secondary to the characteristic inflammatory storm associated with COVID-19 or post-drainage pericardial decompression syndrome.

Patient 3: A 55-year-old African American male with a past medical history of hypertension and obesity presented with 2 weeks of productive cough, myalgias, dyspnea, fatigue, and fever. Labs showed a positive COVID-19 test, bilateral lung opacities and a mildly enlarged cardiac silhouette on CXR. The patient was started on prophylactic dose anticoagulation, intubated for progressive hypoxia on day 2, and required Venovenous extracorporeal membrane oxygenation (ECMO) on day 5. Conditions continued to worsen as the patient developed pulseless electrical activity cardiac arrest on day 7. ECHO revealed a large pericardial effusion with tamponade physiology which was then drained percutaneously. Due to increasing vasopressor and inotropic requirements, a repeat ECHO exhibited biventricular failure. Because of the unlikely paucity of effective aggressive management, all interventions were withdrawn per family’s request; and the patient was pronounced dead.

Case 2: A Case of Hemorrhagic Cardiac Tamponade in a Patient with COVID-19 Infection

The patient is a 62-year-old COVID-19 positive male who presented to the emergency department complaining of progressive shortness of breath and altered mental status. Past medical history included coronary artery disease, hypertension, hyperlipidemia, DM, COPD, alcoholism, and morbid obesity. Noteworthy lab results included an elevated d-dimer, CXR revealed right pleural effusion, and an ECG showed normal sinus rhythm with new low voltage and old left axis deviation. An emergent ECHO showed a large pericardial effusion with tamponade physiology, which was then drained via pericardiocentesis. Other complications of the hospital stay included renal failure, upper GI bleeding, and the development of a lower extremity deep vein thrombosis. Due to the concomitant
pericardial effusion not present on the most recent ECHO, it is presumed that COVID-19 itself caused the pericardial effusion.

**Case 3: Acute Pericarditis and Cardiac Tamponade in a Patient with COVID-19: A Therapeutic Challenge**

A 70-year-old West African female patient presented to the ER with chest pain, worsening dyspnea, and myalgias. Patient has a past medical history of coronary artery disease, type 2 diabetes mellitus, hypertension, hyperlipidemia, and a recent history of non-ST elevation myocardial infarction (NSTEMI) 2 weeks previously. Eventual nasopharyngeal swab returned positive for COVID-19. ECG at presentation showed normal sinus rhythm with T-wave inversions in the inferior leads. CXR showed right basal atelectasis but no effusion and a transthoracic ECHO (TTE) showed normal left ventricular ejection fraction. On day 2, a repeat ECG showed diffuse ST-segment elevations with PR depression suggestive of acute pericarditis. A repeat CXR showed an enlarged cardiac silhouette and bilateral pulmonary infiltrates. A TTE was obtained and revealed a new circumferential fibrinous pericardial effusion, right ventricular diastolic collapse, a dilated inferior vena cava and septal bounce. These findings were consistent with tamponade physiology. Due to hemodynamic instability, an emergent pericardiocentesis was performed.

**Case 4: Cardiac tamponade and massive pleural effusion in a young COVID-19-positive adult**

A 30-year-old male with no past medical history of cardiac illness was diagnosed with COVID-19 after presenting with palpitations, progressive dyspnea, and orthopnea. ECG showed low voltage complexes, and a CXR showed significant enlargement of the cardiac silhouette and a large left pleural effusion. A TTE revealed a large pericardial effusion with right atrial collapse and early signs of right ventricular diastolic collapse, >24% and >40% reduction in mitral inflow and tricuspid inflow velocities, respectively, consistent with cardiac tamponade physiology. After undergoing pericardiocentesis, the patient continued to have dyspnea. CT-thorax showed cardiomegaly with features of pulmonary hypertension and gross pericardial effusion causing compression of left hilum and collapse of the left lung. Based on clinical symptoms, signs, findings on chest-CT, the causes of pericardial and pleural effusions were thought to be due to COVID-19. The patient was discharged on day 5 after showing
fully expanded lungs on CXR and significant resolution of pericardial effusion on 2D ECHO.

**Case 5: A Case of Myopericarditis and Cardiac Tamponade as the Initial Presentation of COVID-19 Infection**

A 57-year-old female with a past medical history of hypertension presented with trouble breathing. EKG showed diffuse ST segment elevations and the initial troponin was noted to be 64.0 mg/ml. Prior to transport to a percutaneous coronary intervention (PCI) center, the patient had cardiac arrest x2 because of hypoxic respiratory failure and was intubated. A COVID-19 PCR test was positive. Bedside ECHO done prior to the coronary angiography showed significant hypertrophy of the left ventricle and moderate pericardial effusion. Laboratory findings were consistent with acute renal failure, shock liver, and high anion gap metabolic acidosis. An official ECHO was done which showed severely reduced EF (15%-25%) and diffuse hypokinesis of the left ventricular wall. The pericardial effusion resolved with the drain in place. The patient’s vasopressor requirement increased throughout the day and became unresponsive to atropine when bradycardic. Blood work did not show any improvement in renal or hepatic function, or in acidosis. ABG showed severe metabolic acidosis (pH 6.90, bicarbonate 3.5) with respiratory alkalosis (PCO2 18.5). Patient had no palpable pulse and was found to be in asystole. Resuscitative efforts were deemed medically futile, and the patient was pronounced deceased.

**Case 6: Cardiac Tamponade Secondary to COVID-19**

A COVID-19 positive 67-year-old woman presented to the ED with worsening dyspnea and orthopnea. Patient had a past medical history of nonischemic cardiomyopathy in 2018 with LVEF of 15% which was managed with guideline-directed medical therapy to which her LVEF was improved to 40%. She was not on antiplatelet agents or anticoagulants and had no history of malignancy. CXR was obtained which showed an enlarged cardiac silhouette and ECG showed low voltage in the limb leads with nonspecific ST-segment changes. TTE revealed a large pericardial effusion circumferentially around the entire heart with signs of early right ventricular diastolic collapse, dilated but collapsing inferior vena cava, and mitral valve inflow variation of 31% on pulsed wave Doppler. Patient’s worsening symptoms, rapid expansion of the effusion,
and the early ECHO findings all pointed to tamponade physiology, which was managed with pericardiocentesis. Fluid cytology was negative for malignant cells, negative on acid-fast bacilli smear, and no growth on cultures. Due to the absence of chest trauma, history of malignancy, or coagulopathy, the hemorrhagic effusion was suspected to be secondary to COVID-19. Upon reported improvements in dyspnea, the patient was discharged from the hospital.

**Case 7: SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade**

A 59-year-old male was admitted to the ED for acute chest pain and was diagnosed with Non-ST Elevation Acute Coronary Syndrome after the discovery of multivessel disease via angiography. Upon undergoing a coronary artery bypass surgery, the patient was extubated, and ECHO showed mild pericardial effusion. Due to the development of dyspnea and fever, a nasopharyngeal swab was tested, confirming the diagnosis of COVID-19. A lung CT was taken showing “ground glass” areas with “crazy paving” pattern in both lungs, alluding to possibility of COVID-19 related interstitial pneumonia. Laboratory results of blood samples showed increasing inflammatory markers (C-reactive protein and fibrinogen), lactic dehydrogenase, and D-dimer which prompted the initiation of low-molecular-weight-heparin (LMWH) and helmet c-PAP for the hypoxic insufficiency. Due to worsening dyspnea and chest pain, a secondary ECHO was performed and documented severe circumferential pericardial effusion conditioning collapse of the right heart. Echo-guided pericardiocentesis was performed and a of the drained fluid was sent for physiochemical, cytological, microbiological, and molecular analysis. Analysis of the patient’s fluid exhibited the SARS-CoV-2 N gene, which confirmed the presence of COVID-19 in the collected pericardial fluid.

**Results**

The novelty surrounding COVID-19 has presented a particular challenge in identifying specific etiologies and risk factors that may lead to the particularly lethal sequelae, such as cardiac tamponade. Analyzing the various presentations and common past medical histories amongst the patients may help demystify the disease process and prognosis. A total of 6 different metrics were used to categorize and quantify the clinical picture. These included demographics (including age and ethnicity), initial clinical presentation; past medical history; number of days between a
patient being diagnosed with COVID-19 and when they develop cardiac tamponade; other reported complications; and the outcome of their hospital stay. Of the 9 total patients discussed above, the average age was 56 years old. Many of the patients had similar comorbidities, including 3 patients with diabetes mellitus, 4 who were obese, and 7 with some form of cardiovascular disease such as coronary artery disease and hypertension. The average time between a positive COVID-19 diagnosis and cardiac tamponade development was approximately 6 days. Of the 9 patients, 6 were discharged after stabilization. While these similarities cannot represent causation, they may be helpful in correlating what pathologies and risk factors physicians should suspect if a patient is presenting with signs of cardiac tamponade.

Table 1

COVID-19 Therapeutics

Due to the novelty of COVID-19, there have not been any curative therapies identified at present. Treatment of both severe and mild cases has been extremely limited, with supportive care being the main therapy option. Supportive care varies depending on the degree of severity but most often includes supplemental oxygen, intravenous fluids, and fever reducers, amongst others. While no antiviral therapies exist, multiple antiviral medications already in use have been used to treat severe COVID-19 infections. Currently, there is no cure for the COVID-19 infection, but the current accepted regimen calls for symptomatic treatment.

In the early days of the pandemic, both hydroxychloroquine and chloroquine had emerged as potential therapies for severe COVID-19 positive patients. The United States Food and Drug Administration had approved emergency use authorization for both drugs due to some promising initial reports of decreased severity of infection following administration. Hydroxychloroquine and chloroquine are traditionally used as anti-malarial drugs, widely known for blocking endosomal mediated fusion for viral entry. Both drugs exhibit some type of anti-inflammatory effect against the virus. However, conflicting case reports have since been reported, with many adverse side effects noted. Q.T. interval prolongation is 1 of the deadliest complications from these medications. This information has proven to be imperative as those patients with cardiac manifestations from COVID-19 should not be prescribed hydroxychloroquine and chloroquine as they might potentially worsen cardiovascular symptoms. Since then, the F.D.A. has revoked the emergency use authorization for both
| Case # | Demographic | Initial Presentation | Past Medical History | Days between COVID-19 Diagnosis and Cardiac Tamponade Development | Other Complications/Sequelae | Outcome |
|--------|-------------|----------------------|---------------------|---------------------------------------------------------------|----------------------------|---------|
| 1-1    | 48-year-old Hispanic Male | Small Pericardial Effusion, Dyspnea | Type 2 Diabetes Mellitus, Morbid Obesity | 8 | None | Discharged |
| 1-2    | 56-year-old Hispanic Male | Chest Pain, Fever, Chills, Cough | None | Within hours | Hypotension, LVEF of 20%, Cardiogenic Shock | Deceased |
| 1-3    | 55-year-old African American Male | Productive Cough, Myalgia, Dyspnea, Fatigue, Fever | Hypertension, Obesity | 7 | Cardiac Arrest, Biventricular failure | Deceased |
| 2      | 62-year-old Male | Altered Mental Status, Progressive Dyspnea | Coronary Artery Disease, Hypertension, Hyperlipidemia, Diabetes Mellitus, COPD, Alcoholism, Morbid Obesity | 2 | Deep Vein Thrombosis, Renal Failure, Upper GI Bleeding | Discharged |
| 3      | 70-year-old West African Female | Chest Pain, Dyspnea, Myalgias | Coronary Artery Disease, Type 2 Diabetes Mellitus, Hypertension, Hyperlipidemia, NSTEMI | 2 | None | Discharged |
| 4      | 30-year-old Male | Palpitations, Dyspnea, Orthopnea | Unspecified cardiovascular disease | 1 | Pulmonary Hypertension | Discharged |
| 5      | 57-year-old Female | Dyspnea | Hypertension | Undisclosed | LVEF of 15% | Deceased |
| 6      | 67-year-old Female | Dyspnea, Orthopnea, Chest Pain, Non-ST | Nonischemic Cardiomyopathy with LVEF of 15% | 7 | None | Discharged |
| 7      | 59-year-old Male | Chest Pain, Non-ST | Coronary Artery Disease | 23 | None | Discharged |
drugs as the risks have outweighed the potential benefits for coronavirus patients.

Anti-inflammatory agents have also been used in the treatment of COVID-19 infection. The proinflammatory mediators such as IL-1, IL-6, and TNF alpha are all implicated in the cytokine storm, which potentiates damage in infected individuals. Therefore, downregulating this inflammatory cascade has been a target for pharmacological treatment. The popular rheumatological agent and IL-6 inhibitor, Tocilizumab, has been used to treat patients with SARS-CoV-2. One such study found that a small dose of tocilizumab was able to increase lung function in 91% of patients.

Both inhaled and systemic corticosteroid usage has increased in an effort to reduce the inflammatory cascade occurring in the lungs and systemically. Studies have proven that 6 mg of dexamethasone or betamethasone have proved effective in lowering mortality in patients who were already on mechanical ventilation. Corticosteroids have become 1 of the mainstays in treatment of COVID-19 positive patients with respiratory failure, however, patients without severe respiratory symptoms do not benefit from corticosteroid use.

Treatment of Cardiac Tamponade

The primary treatment for cardiac tamponade is pericardiocentesis, or the removal of pericardial fluid through needle drainage. However, before proceeding with pericardiocentesis, patients should first be supplied with oxygen with elevated legs. The classical approach to pericardiocentesis is done at the bedside through echocardiography for visualization. Additionally, the patient can undergo fluoroscopy guided pericardiocentesis by utilizing local anesthesia. Pericardiocentesis is an extremely meticulous procedure which requires delicate skill and finesse as the margin for error is quite small. Numerous complications may occur with the most common being ventricular chamber puncture leading to a ventricular arrhythmia. Hemothorax and pneumothorax are additional complications that may arise if pericardiocentesis is not performed properly.

Discussion

Cardiac tamponade is an extremely dangerous condition which can arise from numerous etiology. A gradual buildup of fluid in the pericardial space, such as from inflammatory processes like infection, is better tolerated than acute processes. Acute development of cardiac tamponade such as hemorrhage because of a puncture wound or myocardial
infarction is associated with an increased mortality. While the accumulation of fluid progresses to cardiac tamponade varies, cardiac tamponade secondary to COVID-19 infection most probably develops as a slow process, leading to the development of symptoms later on in the infection rather than earlier. The symptoms of cardiac tamponade individually may overlap with the common symptoms of COVID-19 infection; cough, dyspnea, trouble breathing, and chest pain have all been documented as common symptoms which both pathologies share. Healthcare providers must maintain a high index of suspicion for cardiac tamponade when encountering patients with the aforementioned symptoms. While cardiac tamponade can develop independent of SARS-CoV-2 infection, patients who test positive for this virus must not have their symptoms overlooked when thinking of tamponade as a differential or concurrent diagnosis.

Throughout the COVID pandemic, patients of color and minority populations have had an increased rate of both infection and mortality. Numerous reasons may have caused this, as lack of access to healthcare and pre-existing comorbidities are likely to have played a significant role. These same reasons may be ever present in the development of cardiac tamponade in COVID-19 patients who are minority persons of color. It is also likely that some symptoms may be overlooked in these minorities, which should not be the case. All patients presenting with cardiac tamponade symptoms should be evaluated thoroughly and appropriately in order to minimize mortality.

Additionally, patients who contract COVID-19 and subsequently develop cardiac tamponade may have other risk factors for the development of cardiac tamponade, such as hypertension, obesity, and hyperlipidemia. Hence, it is difficult to unequivocally state the SARS-CoV-2 virus is holistically responsible for the development of cardiac tamponade. However, it may be more appropriate to label this novel coronavirus as an additional risk factor or rather a catalyst for inflammation, which potentiates the accumulation of pericardial fluid and subsequent tamponade. Therefore, it is not our aim to state all COVID-19 positive patients will develop CT but rather present the unique relationship between the 2 distinct pathologies.

**Conclusion**

With the constant evolution of SARS-CoV-2 variant strains, rise in global cases, and the steady progression of the pandemic, it is crucial that any novel disease presentations be documented and researched. Until recently, pericardial involvement has been rarely reported on.
Considering the pathophysiology of COVID-19 and cardiac tamponade, it is plausible that COVID-19, similar to other viral infections, elicits an inflammatory response, leading to pericarditis and subsequent effusion. Our review discusses 9 cases in which cardiac tamponade was a rare complication of COVID-19 infection. Physicians must hold a high index of suspicion when treating patients with cardiovascular decompensation as cardiac tamponade may be a sole, yet potentially lethal manifestation of this novel coronavirus. This article allows providers to be made aware that cardiac tamponade is a rapidly progressing and life-threatening prognosis, and that healthcare providers must be swift to recognize the symptoms and start treatment immediately.

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