A Unique Case of COVID-19-related Acute Coronary Thrombosis Complicated by Severe Hypokalemia

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ABSTRACT We report the case of a 52-year-old white male who was recently diagnosed with symptomatic coronavirus disease-2019 (COVID-19) and presented to the hospital with ventricular tachycardia/ventricular fibrillation cardiac arrest, ST elevation myocardial infarction, and profound hypokalemia. The patient was successfully treated with primary percutaneous coronary intervention and concurrent aggressive potassium repletion. To the authors’ knowledge, this is the first case of COVID-19 presenting not only with an acute coronary thrombosis but also severe hypokalemia, both of which contributed to his cardiac arrest. The association of COVID-19 with acute coronary thrombosis, including the challenges surrounding the diagnosis and management in this patient population, is discussed. Additionally, the effect of COVID-19 on the renin–angiotensin–aldosterone system is reviewed with a focus on hypokalemic presentations.

CASE PRESENTATION

The patient is a 52-year-old white male with a history of hypertension, hyperlipidemia, Barrett’s esophagus, and chronic back pain, who presented to the emergency department with chest pain and, shortly after arrival, developed cardiac arrest. Eight days before this presentation, the patient developed fever, cough, and body aches, and 2 days later he tested positive for coronavirus disease-2019 (COVID-19) by polymerase chain reaction. He did not have any symptoms of vomiting or diarrhea. Approximately 6 days after the onset of symptoms, he began having intermittent substernal chest discomfort that persisted for 2 days until the day of this presentation, when he developed unremitting chest discomfort that prompted his wife to bring him to the emergency department.

Regarding the patient’s relevant past medical history, he had a number of cardiovascular risk factors including hypertension, hyperlipidemia, and pre-diabetes. However, he had no established history of coronary artery disease (CAD) and angina and had no known history of thrombophilia. He was a former tobacco smoker but had quit more than 10 years before presentation. His home medications included rabeprazole 20 mg daily and simvastatin 20 mg daily. Additionally, he was prescribed a course of antibiotics by his primary care physician 1 week prior due to a presumed bacterial pneumonia that he completed 2 days before this presentation.

Once he arrived at the emergency department, he was immediately escorted to an isolation room at which time he lost consciousness. A pulse was not palpable and immediate advanced cardiac life support (ACLS) protocols were engaged. The patient was noted to have multiple unstable dysrhythmias including ventricular fibrillation and pulseless polymorphic ventricular tachycardia (VT). The patient underwent 14 defibrillations for VT/ventricular fibrillation (VF) cardiac arrest. Additionally, the patient was intubated in the isolation room and intravenous epinephrine, magnesium, and amiodarone were given. Upon achieving sinus rhythm with return of spontaneous circulation, the patient was noted to have ST segment elevation in leads I, aVL, V1, and V2 concerning an acute anterolateral myocardial infarction (Fig. 1). A point-of-care ultrasound of the heart confirmed an anteroapical wall motion abnormality consistent with ST elevation myocardial infarction (STEMI). Of note, initial laboratory analysis showed a low serum potassium of 2.6 mmol/L, a low phosphorus of 1.2 mg/dL, and a high-sensitivity troponin of 38 ng/L for which a delta was not obtained. A magnesium level, before the administration of intravenous magnesium during the code, was not obtained. His inflammatory markers, including ferritin, d-dimer, and C-reactive protein, were all elevated, consistent with the known inflammatory state of COVID-19. His serum creatinine and blood urea nitrogen levels were normal. The patient was given aspirin per rectum and an intravenous heparin bolus and emergently taken to the cardiac catheterization laboratory with simultaneous initiation of potassium repletion. Once return of spontaneous circulation was achieved, this patient was noted to be awake and responsive, ultimately requiring sedation in the catheterization laboratory. Targeted temperature management was, therefore, deferred.

Coronary angiography, performed after full personal protective equipment with contact and droplet precautions was donned, revealed single-vessel CAD involving an acute 100% thrombictically occluded proximal left anterior descending (LAD) artery. There was a large amount of thrombus in the proximal LAD artery that extended across the ostium of a moderate-sized second diagonal branch, resulting in TIMI 0 flow in the LAD artery and thrombolysis in myocardial infarction (TIMI) 1 flow in the diagonal branch (Fig. 2). Intravenous cangrelor was administered and, due to the presence of a
FIGURE 1. Electrocardiogram obtained following the return of spontaneous circulation, illustrating ST elevation most notably in leads V1, V2, I, and aVL concerning an ST elevation myocardial infarction (STEMI).

FIGURE 2. Coronary angiography in left anterior oblique (LAO) caudal projection, illustrating a 100% thrombically occluded proximal left anterior descending (LAD) artery and subtotal occlusion of the second diagonal branch vessel.

large amount of thrombus, aspiration thrombectomy was performed. TIMI 3 flow in the LAD artery and diagonal branch was subsequently restored with a door to revascularization time of 101 min. A 3.0 × 24 mm Synergy Drug-eluting Stent was then successfully deployed using intracoronary ultrasound guidance (Fig. 3). Unfortunately, despite the aggressive use of microvascular vasodilators, flow into the apical LAD artery and diagonal branch remained suboptimal with minimal myocardial blush that was suspected to be multifactorial with contributions from persistent microvascular obstruction and myocardial edema. The patient was, consequently, started on an eptifibatide infusion in an attempt to further improve microvascular flow, pharmacologically. Although a cardiac MRI was entertained to inform prognosis, it was deferred in favor of minimizing the number of healthcare providers exposed to COVID-19. Residual, mild-to-moderate CAD of the mid LAD artery and first diagonal branch up to 40–50% was otherwise noted and deferred to medical management.

The patient was transferred to the ICU using appropriate COVID precautions and successfully extubated within an hour of case completion. A repeat EKG was performed and revealed evidence of an anteroseptal and anterolateral infarct with improved, albeit, persistent ST elevation. A chest X-ray obtained at that time showed worsening multifocal
with stable New York Heart Association Class II symptoms for his CAD and heart failure with reduced ejection fraction on maximally tolerated guideline-directed medical therapy stable left ventricular ejection fraction of 35–40%. He remains echocardiogram performed 3 months after discharge showed a any defibrillation by his life vest. A repeat transthoracic ics. The patient did well after discharge and did not require close follow-up in the heart failure and infectious disease clin-
apy. He was discharged with a life vest on hospital day 10 with the next several days, continued to improve on medical ther-
infarction was initiated.

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![FIGURE 3](https://example.com/figure3.png)  
**FIGURE 3.** Repeat coronary angiography after successful placement of a 3.0 × 24 mm Synergy Drug-eluting Stent in the proximal left anterior descending (LAD) artery.

airspace opacities as compared to one performed 6 days before admission. He was started on dual antiplatelet therapy with aspirin and ticagrelor and his cangrelor infusion was dis-

The patient was transferred to the step-down unit and, over the next several days, continued to improve on medical ther-

and no evidence of VT on monitoring. The placement of an implantable cardioverter-defibrillator was therefore deferred and his life vest was discontinued.

**DISCUSSION**

This case highlights the acute cardiovascular morbidity associated with COVID-19 infection with specific attention to the increased risk of acute coronary thrombosis. Additionally, although acute, thrombotically occluded proximal LAD artery contributed to the initial cardiac arrest, the profound presenting hypokalemia provided a firm foundation for further electrical instability in this setting and underscores the detri-

Coronavirus disease-2019 is caused by a novel enveloped RNA *Betacoronavirus* that has been named severe acute respira-

tory syndrome coronavirus 2 (SARS-CoV-2). This virus enters human cells primarily through angiotensin converting enzyme 2 (ACE2) binding. This enzyme is primarily expressed in alveolar cells, cardiac myocytes, and vascular endothelium.3 Although respiratory symptoms are the primary clinical manifestation of COVID-19, a variety of cardiovascular complications can occur including acute coronary thrombosis, acute myocardial injury without obstructive CAD, arrhythmias, heart failure (with or without cardio-

demonstrate the morbid interplay of simultaneous, COVID-

The frequency, relative incidence, and phenotype of COVID-19-related acute coronary thrombosis versus other associated cardiac manifestations are not well defined.3 Recent studies have highlighted that not all symptomatic COVID-19 cases with focal ST elevation on EKG are sec-

Another paper reviewed the cases of 28 coronavirus-positive patients admitted for STEMI showed 11 of these patients did not have obstructive CAD (39.3%).4 Another paper reviewed the cases of 18 patients with COVID-19 and STEMI, of which 50% under-

The initial management of confirmed or suspected COVID-19-positive patients who present with ST elevation on EKG, therefore, can pose a management dilemma in the emergency department. On the one hand, performing emergent coronary angiography on all patients with presenting ST elevation on EKG provides unnecessary viral exposure to the cardiac catheterization team in cases without an acute coronary thrombosis and poses unnecessary risks to the patient by performing a procedure they did not otherwise need. On the other hand, a missed or delayed diagnosis of an acute coronary thrombosis in the setting of non-specific symptoms can increase short- and long-term cardiovascular morbidity and
mortality. Indeed, one of the ways these risks have been mitigated is with the use of systemic thrombolysis in suspected or confirmed COVID-19 patients presenting with a possible STEMI. However, given the data supporting primary percutaneous coronary intervention over thrombolysis as a means to reduce death, non-fatal re-infarction, and stroke and the increased risk of bleeding associated with thrombolytic therapy, a thrombolytic strategy for all COVID-19 patients with ST elevation presenting at hospitals capable of percutaneous coronary intervention is not being routinely recommended in the USA. Alternatively, the use of point-of-care ultrasound to assist in the immediate management of these patients can be helpful with the presence of focal wall motion abnormalities used to decide if the patient should be taken emergently to the cardiac catheterization laboratory. Of note, laboratory values including high-sensitivity troponin or C-reactive protein may be of little benefit in distinguishing between acute coronary thrombosis and an STEMI mimic in the setting of COVID-19, as these laboratory values are likely to be elevated for a number of different reasons in infected patients. As such, the decision to proceed with coronary angiography should take into account the patient’s pre-test probability for CAD, ultrasound imaging if obtained, and resource availability.

Outside of the existing guidelines for management of acute coronary thrombosis, evidence-based treatment of COVID-19-associated acute coronary thrombosis is limited. However, potential drug interactions between current therapies for acute coronary thrombosis and investigational therapies for COVID-19 are worthy to note and, thus, may require a more thoughtful approach to what specific acute coronary thrombosis therapies are chosen. Although no known interactions between parenteral antithrombotic therapies and investigational therapies for COVID-19 are known to exist, potential interactions between antiplatelet therapies used in acute coronary thrombosis and those therapies used in COVID-19 do exist as a result of the co-interaction with the cytochrome system. Lopinavir/ritonavir inhibits CYP3A4 metabolism, which can lead to a reduction in the effective dosage of clopidogrel or actually increase the effects of ticagrelor. Remdesivir, a nucleoside analog inhibitor of RNA-dependent RNA polymerase, is an inducer of CYP3A4 but does not currently require dose adjustments for oral antiplatelet medications. Tocilizumab, an interleukin-6 inhibitor, results in increased expression of CYP3A4 and 2C19 with no dose adjustments on oral antiplatelet agents currently recommended. Sarilumab, which inhibits interleukin-6-mediated signaling, also increases expression of CYP3A4 but with no dose adjustments on currently recommended oral antiplatelet agents. Other investigational therapies including azithromycin, bevacizumab, hydroxychloroquine, eculizumab, interferon, losartan, methylprednisolone, pirfenidone, and ribavirin are not currently identified as having drug–drug interactions with antiplatelet agents. Although the propensity of COVID-19 to cause thromboses has been well described, the association with hypokalemia is only recently being recognized. Severe acute respiratory syndrome coronavirus 2 enters human cells primarily through ACE2 binding, an enzyme that plays an important role in angiotensin II regulation. Under normal conditions, ACE converts angiotensin I to angiotensin II that can then exert multiple angiotensin II type 1 receptor-mediated effects, including increased water reabsorption and production of aldosterone, which increases sodium resorption and enhances potassium secretion. Angiotensin converting enzyme 2 counteracts ACE, converting angiotensin II to angiotensin I–VII, thus prohibiting angiotensin II from initiating its downstream effects. The downregulation of ACE2 as a consequence of SARS-CoV-2 binding and SARS-CoV-2 viral mediators can therefore shift the balance between these two enzymes and contribute to a relative state of hyperaldosteronism with subsequent hypokalemia as exhibited by our patient. Data are limited, but there is currently one prospective cohort study evaluating the prevalence of hypokalemia and response to treatment with potassium supplementation in patients with COVID-19. One hundred and seventy-five patients were enrolled. Eighteen percentage of patients had potassium less than 3 mmol/L and 37% had potassium less than 3.51 mmol/L, overall indicating a high prevalence of hypokalemia in this population. Patients responded well to potassium supplementation. Additionally, more severe hypokalemia appeared to be associated with more severe disease activity. Among those with severe hypokalemia, only 29% had diarrhea, and there was no difference between those with and without diarrhea. As noted by the study authors, this finding suggests that hypokalemia is a result of renal losses as opposed to gastrointestinal losses, thereby underscoring the theory of an acquired state of hyperaldosteronism.

When considering other potential contributors to this patient’s hypokalemia, it should be mentioned that, although he did not have symptoms of vomiting or diarrhea before this presentation, he was on hydrochlorothiazide 25 mg daily, which could lead to hypokalemia by way of potassium excretion by the kidney, given its diuretic properties. It is unclear what role, if any, this medication had on the potassium level before and at the time of this presentation as the most recent laboratory values were from 2 years prior. Future research could evaluate these associations to help inform both inpatient and outpatient management of patients with COVID-19.

CONCLUSION
Coronavirus disease-2019 is a pro-thrombotic illness that may increase the likelihood of acute coronary thrombosis. Additionally, ACE2 downregulation by SARS-CoV-2 can have deleterious effects on the balance of the renin–angiotensin–aldosterone axis promoting hypokalemia. This case represents the first known case of both of these COVID-19-related complications acting synergistically to cause VT/VF
arrest. Indeed, an increased incidence of out-of-hospital cardiac arrest has been seen in the COVID era. Although this is likely multifactorial from increased risk of COVID-related respiratory failure, coronary and pulmonary thromboses, myocarditis, dysrhythmia, and a possible hesitancy to seek emergent health care amidst a global pandemic, the associated profound electrolyte abnormalities seen as a direct result of the deleterious effect of COVID-19 on the renin–angiotensin–aldosterone system cannot be ruled out as a potential contributor.

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**CONFLICT OF INTEREST STATEMENT**
We have no conflicts of interest to disclose.

**REFERENCES**
1. Prieto-Lobato A, Ramos-Martínez R, Vallejo-Calcerrada N, Corbí-Pascual M, Córdoba-Soriano JG: A case series of stent thrombosis during the COVID-19 pandemic. JACC: Case Rep 2020; 2(9): 1291–96.
2. Bikdeli B, Madhavan MV, Jimenez D, et al: COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. J Am Coll Cardiol 2020; 75(23): 2950–73.
3. Hendren NS, Drazner MH, Bozkurt B, Cooper LT Jr.: Description and proposed management of the acute COVID-19 cardiovascular syndrome. Circulation 2020; 141: 1903–14.
4. Stefanini GG, Montorfano M, Trabattoni D, et al: ST-elevation myocardial infarction in patients with COVID-19: clinical and angiographic outcomes. Circulation 2020; 141(23): 2113–6.
5. Bangalore S, Sharma A, Slotwiner A, et al: ST-segment elevation in patients with Covid-19—a case series. N Engl J Med 2020; 382(25): 2478–80.
6. Jing ZC, Zhu HD, Yan XW, Chai WZ, Zhang S: Recommendations from the Peking Union Medical College Hospital for the management of acute myocardial infarction during the COVID-19 outbreak. Eur Heart J 2020; 41(19): 1791–4.
7. Keeley EC, Boura JA, Grines CL: Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet (London, England) 2003; 361(9351): 13–20.
8. Mahmud E, Dauerman HL, Welt FG, et al: Management of acute myocardial infarction during the COVID-19 pandemic. J Am Coll Cardiol 2020; 76(11): 1375–84.
9. The American Heart Association’s Get With The Guidelines-Coronary Artery Disease Advisory Work G, Mission Lifeline P, The American Heart Association’s Council On Clinical C, The American Heart Association’s Council On Clinical Cardiology’s Committee On Acute Cardiac C, General Cardiology C and The American Heart Association’s Council On Clinical Cardiology’s Committee Interventional Cardiovascular Care C: Temporary emergency guidance to STEMI systems of care during the COVID-19 pandemic: AHA’s mission: lifeline. Circulation 2020; 142(3): 199–202.
10. Madjid M, Safavi-Naeini PS, Solomon SD: Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol 2020; 5(7): 831–40.
11. Klok FA, Kruip M, van der Meer NJM, et al: Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020; 191: 145–7.
12. Lodigiani C, Iapichino G, Carenzo L, et al: Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res 2020; 191: 9–14.
13. Helms J, Tacquard C, Severac F, et al: High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med 2020; 46(6): 1089–98.
14. Groll S, Jahn C, Cushman S, Bär C, Thum T: SARS-CoV-2 receptor ACE2-dependent implications on the cardiovascular system: from basic science to clinical implications. J Mol Cell Cardiol 2020; 144: 47–53.
15. Brojakowska A, Narula J, Shimony R, Bander J: Clinical implications of SARS-CoV-2 interaction with renin angiotensin system: JACC review topic of the week. J Am Coll Cardiol 2020; 75(24): 3085–95.
16. Chen D, Li X, Song Q, et al: Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. JAMA Network Open 2020; 3(6): e2011122.
17. Baldi E, Sechi GM, Mare C, et al: COVID-19 kills at home: the close relationship between the pandemic and the increase of out-of-hospital cardiac arrests. Eur Heart J 2020; 41(32): 3045–54.