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## Syncope Associated with Sinus Nodal Dysfunction in a COVID-19 Patient: A Case Report and Review of the Literature

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### Abstract

COVID-19 caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is associated with significant cardiovascular dysfunction in patients with, and without, pre-existing cardiovascular disease [1]. There are now well-documented cardiac complications of COVID-19 infection which include myocarditis, heart failure, and acute coronary syndrome [2]. There is growing evidence showing that arrhythmias are also one of the major complications of COVID-19. We report a patient with no known cardiac conduction disease who presented with syncope, positive SARS-CoV-2 PCR, who was persistently bradycardic and subsequently developed sinus node dysfunction (SND). To date, there are a limited number of reports of sinus node dysfunction (SND) associated with COVID-19. We describe the clinical characteristics, potential pathophysiologic mechanisms and management of COVID-19 patients who experienced de novo SND.

### Keywords

COVID-19; SARS-CoV-2; bradycardic; sinus node dysfunction (SND)

### 1. Introduction

On January 7, 2020, a novel coronavirus, originally abbreviated as 2019-nCoV by the World Health Organization (WHO), was identified from a throat swab sample. This pathogen was later renamed the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by the Coronavirus Study Group, and the disease was named coronavirus disease 2019 (COVID-19) by the WHO [3].

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Since the inception of the pandemic, we have continuously learned more and more about the cardiovascular complications of Coronavirus disease 2019 (COVID-19), which include myocardial infarction, myocarditis, stroke, tachyarrhythmias and pulmonary embolism. To date, less is known about the prevalence, clinical characteristics and outcomes of arrhythmias in patients with COVID-19.

Recent literature has demonstrated that COVID-19 may be associated with cardiac conduction abnormalities, however, there has only been speculation on the exact mechanism. At the time of writing this manuscript, there have only been a few reported cases of inappropriate sinus bradycardia associated with COVID-19. In this report, we describe a case of COVID-19 affecting the cardiac conduction system of an elderly female resulting in pathological SND. We explore and investigate COVID-19 and its impact on the cardiac conduction system.

## 2. Case Description

An 84-year-old female with PMHx significant for HTN, IDDM, HFpEF, CAD s/p PCI w/ DES, CKD, presented to the hospital with syncope. There was no head trauma, seizure activity, tongue biting or urinary/fecal incontinence per daughter, who witnessed the episode. At baseline, the patient has dyspnea on exertion, orthopnea, PND and lower extremity swelling bilaterally. She had endorsed abdominal discomfort for multiple days prior to the event. There were no recent sick contacts or recent travel and she denied cough, fever, chills or diarrhea.

In the Emergency Department (ED), initial blood pressure was stable with a HR of 50 bpm. Her cardiovascular exam was unremarkable and the respiratory exam was notable for inspiratory crackles at the bases bilaterally. Initial labs were pertinent for mildly elevated inflammatory markers (Table 1). She received IV lasix and required 2 L/min of nasal cannula to maintain adequate SpO<sub>2</sub>. A chest radiograph showed a small left-sided pleural effusion. Nasopharyngeal PCR was positive for COVID-19.

An electrocardiogram (EKG) confirmed sinus bradycardia, HR 45 bpm with no AV-node dysfunction (Figure 1). Transthoracic echocardiogram (TTE) on admission demonstrated an ejection fraction (EF) of 60%, no wall motion abnormalities and mild aortic stenosis (AS). Cardiac enzymes negative x2. Coronary angiogram from 2014 showed single vessel thrombotic occlusion of the marginal branch of the right coronary artery (mRCA).

On day 3 of hospitalization, she developed worsening renal failure and hypoxemia, requiring 6L of oxygen via nasal cannula to maintain O<sub>2</sub> saturation. Telemetry monitoring continued to show persistent sinus bradycardia with a nadir of 40 bpm. At this time, the patient remained afebrile, hemodynamically stable. Electrolytes and thyroid stimulating hormone (TSH) were within normal limits. All atrioventricular (AV) nodal blocking agents were held. No ST segment changes or T-wave abnormalities were identified on serial EKGs and cardiac biomarkers remained negative. Additionally, the patient never endorsed any chest pain or pressure during the hospital course.

Given the persistent sinus bradycardia recorded on cardiac telemetry, a decision was made to undergo an electrophysiology (EP) study which revealed a delayed sinus node recovery time (Figure 2), confirming SND. Subsequently, a dual chamber permanent pacemaker (PPM) was successfully placed without complications. Upon further evaluation, she was recommended for subacute rehab (SAR) with outpatient cardiology follow up.

### 3. Discussion

Sinus node dysfunction (SND) includes a spectrum of heart rhythm disturbances related to abnormal sinus impulse formation or propagation and has different presentations, such as bradycardia, alternating episodes of bradycardia and tachycardia and sinoatrial block. Sick sinus syndrome most commonly affects the elderly but can affect all age groups. Patients typically present with syncope or near syncope, palpitations, dizziness, or fatigue, but patients may also be asymptomatic in the early phase of the disease. When symptoms are related to dysfunction of the sinus node, treatment consists of correcting underlying causes and inserting a permanent pacemaker [4].

The relationship between SARS-CoV-2 infection and sinus node dysfunction is not well understood. To date, numerous mechanisms have been postulated, which include but are not limited to a robust systemic inflammatory response, direct viral cytotoxic effect of the cardiac myocyte, and autonomic dysfunction via invasion of the CNS altering the cardio-respiratory center within the brainstem.

Recent literature has suggested that myocardial injury is common in critically ill COVID-19 patients. Myocarditis secondary to a robust systemic inflammatory response via cytokine release (interleukin-6 and tumor necrosis factor- $\alpha$ ) are unlikely to cause sinus node dysfunction in our patient due to the mild inflammatory markers, normal troponin indicating less likely to have myocardial injury, and preserved cardiac function seen on the transthoracic echocardiogram (TTE).

SARS-CoV-2 has an affinity for the angiotensin-converting enzyme 2 (ACE2) receptor located on the cardiac myocyte. Autopsies of patients who died secondary to COVID-19 have shown the presence of viral RNA in cardiac myocytes and endothelial cells suggesting direct involvement of the myocardium in this disease [4,5], Direct viral cytotoxic effect on the cardiac myocyte via ACE2 receptor was unlikely a cause of SND in the setting of negative cardiac biomarkers, indicating no direct damage to the cardiomyocyte.

Increasing evidence shows that coronavirus (CoVs) may also invade the CNS. The development of SND may be a result of autonomic dysfunction or alteration of the medullary cardio-respiratory center via synapses of the chemoreceptors and mechanoreceptors found in the lower respiratory airways. Considering that most CoVs share a similar viral structure and infection pathway, the infection mechanisms previously found for other CoVs may also be applicable to SARS-CoV-2 [6].

In fact, the intrinsic cardiac nervous system has regional control over different cardiac functions, such as sinus node electrical activation and propagation, as well as atrioventricular nodal conduction, and consists of ganglia composed of afferent, efferent, and

interconnecting neurons to other cardiac ganglia. These ganglia coordinate the sympathetic and parasympathetic inputs received from the rest of the cardiac autonomic nervous system [6].

Given the patient's presentation, special attention was given to both intrinsic and extrinsic cardiac causes of sinus node dysfunction [7], Initial chemistry was unremarkable and electrolytes were repleted daily throughout the hospital course. All nodal blocking pharmacologic agents were held in the setting of persistent bradycardia. Differential diagnosis included hypothyroidism, however, thyroid stimulating hormone (TSH) was within normal limits. Intrinsic causes were less likely to be a cause due to transthoracic echocardiogram revealing an EF of 60% with no wall motion abnormalities. There was very low suspicion for ischemia as the underlying precipitant. Serial electrocardiograms (EKG's) and cardiac troponin-I x3 didn't indicate any active ischemic changes in the setting of no active chest pain or anginal equivalent during the admission. Furthermore, per chart review, cardiac catheterization report indicated a lesion of the marginal branch of the right coronary artery (mRCA), which is distally located and supplies the lateral right ventricular wall; inconsistent with the development of SND. Working diagnosis at this time was autonomic dysfunction secondary to COVID-19 infection.

Once reversible causes were excluded, an electrophysiology study confirmed SND. Symptoms were related to dysfunction of the intrinsic sinus node, and the patient underwent dual-chamber rate-modulated implantation of a pacemaker (PM).

Patients diagnosed with COVID-19 should be monitored closely for the development of bradyarrhythmia and hemodynamic instability. Additionally, we noted that our patient's persistent bradyarrhythmia didn't improve throughout the hospital course and occurred with evidence of continuous viremia and virus shedding, given the persistence of positivity of two nasopharyngeal PCR SARS-CoV-2 tests over the patient's full admission period, suggesting a correlation of the bradyarrhythmias to SARS-CoV2 infection [3].

As we continue to learn the pathophysiology of COVID-19, it's still not clear if SARS-CoV-2 can cause reversible cardiac conduction disease of the sinus node. In the absence of clear guidelines, physicians are to use their own clinical judgment when deciding on the time to allow for the sinus node to recover. We cautiously monitored our patient on cardiac telemetry, however due to the persistent bradyarrhythmia and confirmed EP study of SND, a permanent dual chamber pacemaker was placed.

#### 4. Conclusion

This case was specifically selected because despite the reported history of a normal conduction system and the lack of nodal blocking agents along with normal initial tests including ECGs, electrolytes, and echocardiography, the patient developed persistent bradyarrhythmias [2]. To the best of our knowledge, only a few similar cases have been described in the literature since COVID-19 was identified. Although the most common cause of sinus node dysfunction is degenerative fibrosis, we speculate that this novel virus traumatizes the central nervous system inducing autonomic dysfunction with subsequent

cardiac conduction abnormalities. Future studies are needed to isolate this exact mechanism and guide our management.

## Acknowledgements

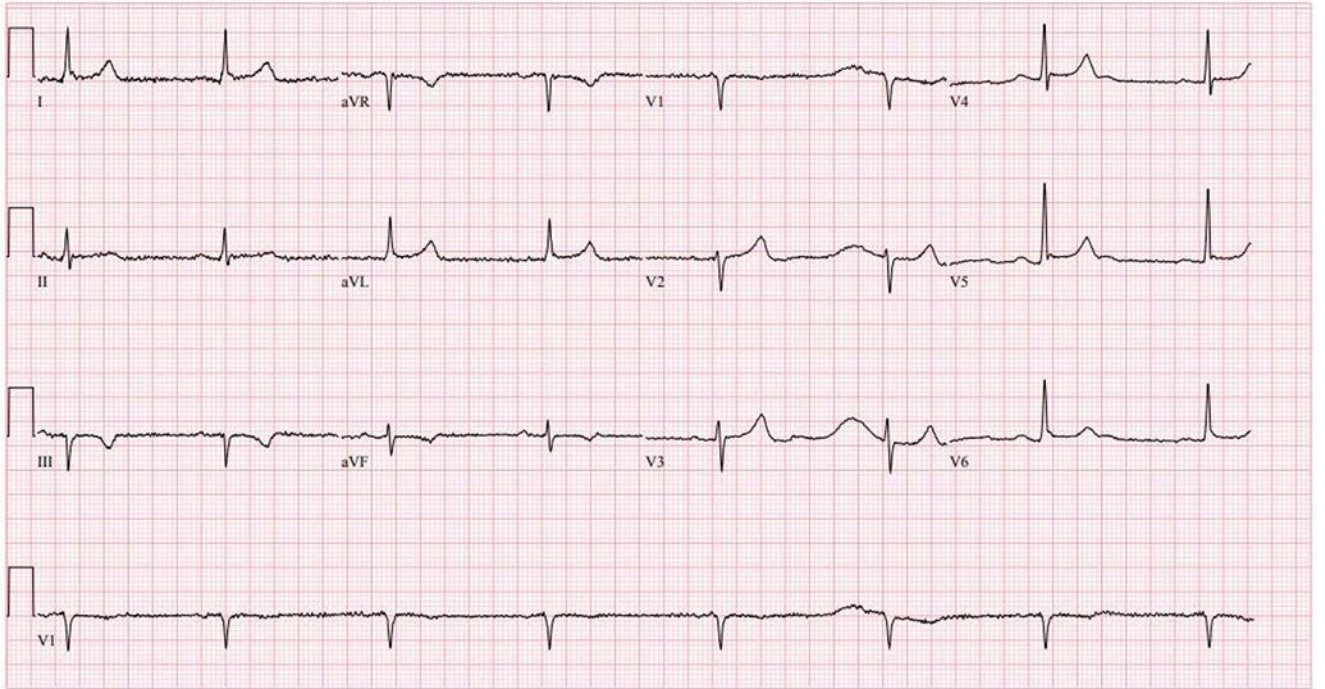
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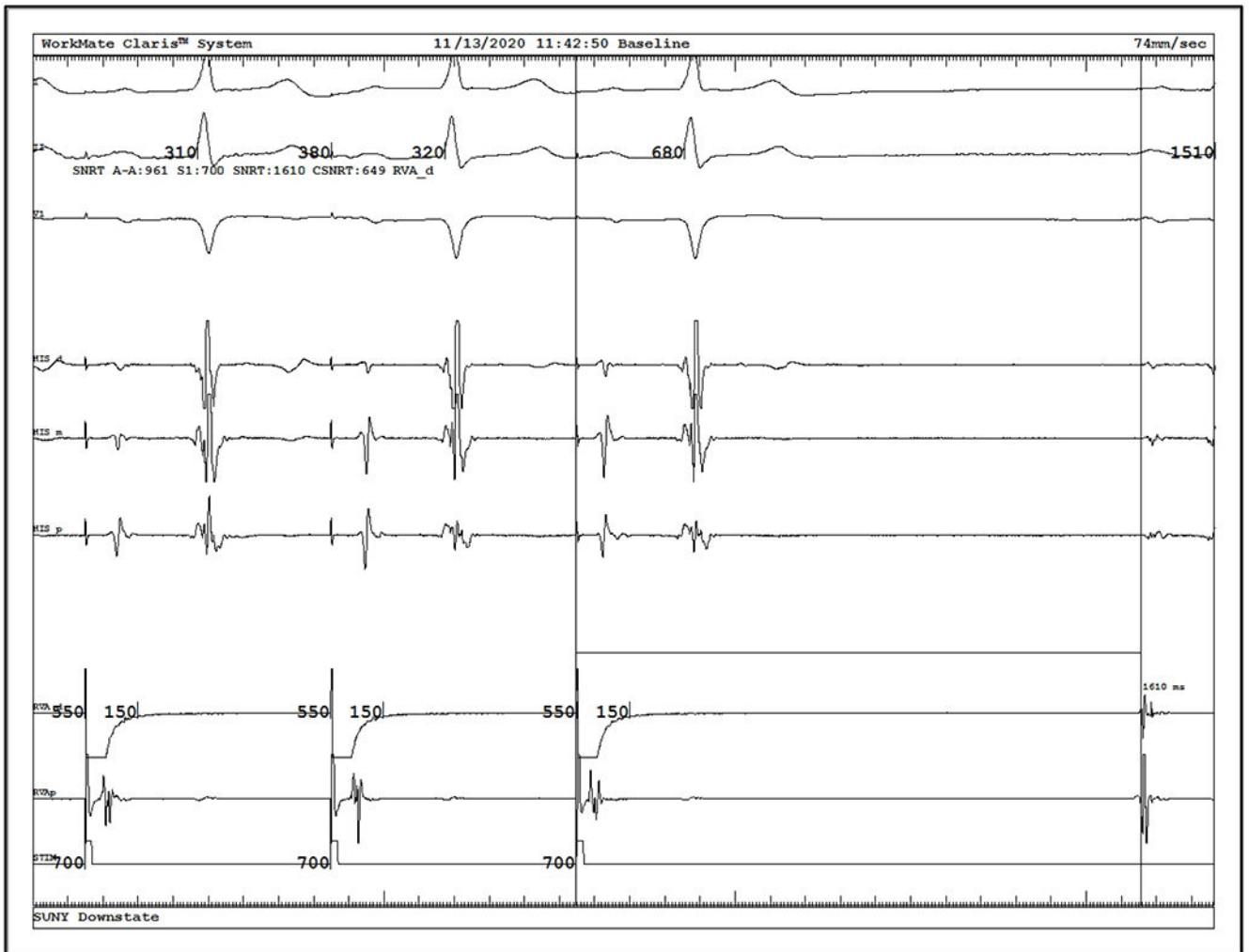
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### Teaching Points

- Novel coronavirus disease-19 (COVID-19) may cause sinus node dysfunction (SND).
- The mechanism for COVID-19-induced sinus node dysfunction (SND) is likely to be secondary to cardiac inflammation, direct viral infiltration of cardiac myocyte via ACE2 receptor and invasion of the CNS causing autonomic dysfunction.
- Patients with COVID-19 should be monitored closely for development of bradyarrhythmia and hemodynamic instability.



**Figure 1.**  
EKG, Sinus Bradycardia HR 45bpm



**Figure 2.** Corrected sinus node recovery time (CSNRT) is 629 ms (normal < 525 ms ). CSNRT is greater than 100ms from the upper limit of normal, which is specific to SND; RVA: right ventricle catheter placed in the high right atrium; A-A: sinus rhythm cycle length



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Table 1.

Laboratory Results During Hospital Admission

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
WBC	8.6	6.7	9.1	8.4	7.0	11						10
Hgb	8.3	8.5	7.6	8.0	7.8	7.4						7.8
Plt	267	287	300	254	298	305						195
Na	132	134	132	132	127	138						135
K	5.3	5.5	5.5	5.5	6.6	5.1						5.5
Cl	104	104	101	101	101	103						92
HCO3	23	22	22	21	16	29						35
BUN	43	47	51	69	71	63						45
Cr	1.4	1.5	1.7	2.8	2.4	1.8						2.2
Glucose	222	92	299	68	225	139						209
Mg		2.2		2.3	2.4							2.1
PO4		4.7										
Ca	8.7	8.7	8.2	7.9	7.8	7.8						8.6
Troponin-I	0.02	0.02	0.02									
BNP	368			122	249							
Lactic Acid	1.0											
pH	7.32				7.26							
ProCalcitonin		Undetected				Undetected						
Ferritin		44		27		30						
DDHS 500			1444									
LDH		258				167						
CPK		59										
ESR						34						
CRP		58				10						
HgA1c		8.9										
TSH	WNL											
PT / INR / aPTT	1 / 12.4 / 28											

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	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
RVP	Undetected											
COVID PCR	Positive						Positive				Undetected	