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RESEARCH CORRESPONDENCE

Atrial Arrhythmias in COVID-19 Patients

The COVID-19 global pandemic presents with a wide range of clinical manifestations, including biochemical, echocardiographic, and electrocardiographic (ECG) evidence of myocardial involvement (1–3). However, the occurrence of atrial arrhythmias in patients with this infection and how these arrhythmias impact the clinical course of patients with COVID-19 has not been well described. In an Institutional Review Board–approved protocol, we analyzed the 12-lead ECGs and telemetry of all patients admitted to the University of Alabama at Birmingham Hospital between February 29, 2020, and April 10, 2020, with polymerase chain reaction–proven SARS-CoV-2 infection.

There were 115 patients admitted with COVID-19, including 69 patients admitted to the medical intensive care unit (MICU) and 46 patients admitted to a general medicine ward. The age was 56 ± 17 years, including 54% men. There were 64 African American, 41 White, and 10 Asian or Hispanic individuals. Underlying comorbidities included hypertension in 70%, current or former tobacco use in 42%, diabetes in 39%, coronary artery disease in 16%, chronic kidney disease in 14%, and chronic obstructive lung disease in 13%. An atrial tachyarrhythmia that had not been present on admission was recorded on a subsequent 12-lead ECG in 19 patients (16.5%), all admitted to the MICU (27.5% of MICU patients). In contrast, no patient admitted to the general inpatient service developed atrial arrhythmias ($p = 0.00002$). These arrhythmias included atrial fibrillation in 12 patients, atrial flutter in 6 patients, and atrial tachycardia in 1 patient.

Compared with patients without atrial tachyarrhythmias, those with atrial fibrillation, flutter, or tachycardia tended to be older with higher concentrations of C-reactive protein (CRP) and d-dimer, but had similar levels of brain natriuretic peptide (BNP) and high-sensitivity troponin (Table 1). Five MICU patients reported a history of atrial fibrillation before admission, including 3 of 19 who developed atrial arrhythmias and 2 of 50 who did not ($p = 0.12$). Although not reaching statistical significance, patients of white race tended to have a higher risk of developing atrial arrhythmias. Prior use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers was similar among patients with and without atrial arrhythmias. No difference was observed in the occurrence of atrial arrhythmias with the use of remdesivir, hydroxychloroquine, or azithromycin.

TABLE 1 Characteristics of Patients With and Without Atrial Arrhythmias

	Atrial Arrhythmias (n = 19)	No Atrial Arrhythmias (n = 96)	p Value
Age, yrs	64.6 ± 12.8	55.8 ± 17.0	0.028
BMI, kg/m^2	29.0 ± 7.7	31.9 ± 10.3	0.27
Male	13 (68)	49 (51)	0.17
Race (Black/White/other)	9/10/0	59/31/6	0.11
Required ventilation	16 (84)	36 (38)	0.0002
Prior atrial fibrillation	3 (16)	3 (3)	0.06
HTN	14 (74)	66 (69)	0.67
CAD	3 (16)	20 (21)	0.62
Systolic heart failure	2 (11)	5 (5)	0.33
Diastolic heart failure	4 (21)	16 (17)	0.74
ACEI/ARB	5 (26)	30 (31)	0.79
CRP, mg/l	220 ± 162	138 ± 108.3	0.084
BNP, pg/ml	495 ± 833	329 ± 621	0.33
HS troponin, ng/l	793 ± 10,741	546 ± 21,723	0.08
D-dimer, ng/ml	5,177 ± 6,706	3,610 ± 4,517	0.41
Remdesivir/placebo trial	1 (5)	7 (7)	1.0
Hydroxychloroquine	2 (11)	5 (5)	0.33
Azithromycin	11 (58)	39 (41)	0.21
Vasopressor data			
Vasopressor use	15 (79)	33 (34)	0.001
Days on vasopressors	5 ± 5	1 ± 3	0.001
Maximum NE Eq	0.20 ± 0.18	0.08 ± 0.18	0.05

Values are mean ± SD or n (%). Comparisons are Fisher's exact test for categorical values and the nonparametric Mann-Whitney *U* test for continuous variables.

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; BNP = brain natriuretic peptide; CAD = coronary artery disease; CRP = C-reactive protein; HS = high-sensitivity; HTN = hypertension; NE Eq = norepinephrine equivalents.

The requirement for mechanical ventilation was strongly associated with the development of atrial arrhythmias ($p = 0.0002$). Vasopressors were required to support blood pressure at some point during the hospitalization in 47 (68%) of 69 MICU patients, including 15 (79%) of 19 patients with and 32 (64%) of 50 patients without atrial arrhythmias. Ten of 19 patients experienced hemodynamic compromise within 1 h of the onset of an atrial arrhythmia, including 9 patients who required initiation or increased dose of vasopressors and 1 patient who required immediate direct current cardioversion. Seven (37%) of 19 patients who developed an atrial arrhythmia were receiving a vasopressor infusion at the onset of the arrhythmia. This was followed by hemodynamic deterioration (increased vasopressor dose requirement or direct current cardioversion) within 1 h in all 7 patients. The equivalent dose of norepinephrine for all vasopressors was standardized as previously

reported (4), with a conversion factor of 1 ng angiotensin II per 0.1 μg of norepinephrine used based on the ATHOS-3 (Angiotensin II for the Treatment of High-Output Shock 3) trial (5). For the 9 patients who had a new or increased vasopressor requirement, the mean change in norepinephrine-equivalent dose requirement was 0.21 μg/kg/min. Five patients with atrial tachyarrhythmias did not require initiation of vasopressors. At the time of analysis, the mean duration of atrial tachyarrhythmias was 6.9 ± 7.3 days and the duration that vasopressors were required was significantly longer for patients with atrial arrhythmias.

In addition to atrial tachyarrhythmias, new inferior and lateral ST-segment elevation or depression and/or T-wave inversions were observed in 19 of the total population of 115 patients, including 7 (15.2%) of 46 patients admitted to the general medical service and 12 (17%) of 69 patients admitted to the MICU ($p = 0.74$). The mean serum troponin was 736 ± 2604 ng/l in patients with ST-segment abnormalities compared with 565 ± 1,506 ng/l without ST-segment changes ($p = 0.24$). There was no significant difference in serum BNP, CRP, or d-dimer levels comparing patients with and without ST-segment abnormalities. In addition, there was no correlation between ST- and T-wave abnormalities and the occurrence of atrial arrhythmias ($p = 0.74$).

The treatment of atrial arrhythmias included intravenous amiodarone in 9 patients with 7 converting to sinus rhythm. One patient who received direct current cardioversion reverted to atrial fibrillation within minutes. Because of contraindications, including bleeding, anticoagulation was administered to only 12 of 19 patients. Ultimately, of the 19 patients with atrial arrhythmias, 5 patients died (26.3%), 10 were discharged in sinus rhythm, and 4 discharged in atrial fibrillation.

Atrial arrhythmias are common among patients with COVID-19 who require admission to an intensive care unit and are often followed by hemodynamic deterioration. These arrhythmias complicate the course of the more severely ill patients with this infection.

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TO THE EDITOR

Debating the Definition and Incidence of Isolated Cardiac Sarcoidosis

We read with interest the paper by Hoogendoorn et al. (1) and congratulate them on their superb contribution; however, we have 3 comments. The first is to ask for a clarification of the following statement: "Thirteen (93%) cardiac sarcoidosis (CS) patients had extracardiac involvement. However, if excluding extracardiac findings, only 6 (43%) CS patients would have been diagnosed correctly as isolated CS based on the Japanese 2017 criteria." The second is to emphasize the key importance of atrioventricular block in distinguishing between cardiac sarcoidosis (CS) and arrhythmogenic right ventricular cardiomyopathy (ARVC). Philips et al. (2) reported 15 patients who were positive for ARVC by Task Force criteria and were subsequently found to have CS and compared