Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Research Letter

Impact of Bradyarrhythmias Requiring Pacing on Outcomes in Patients With COVID-19

Brady-arrhythmias are recognized as a major complication of COVID-19.[1-3] Studies have described rates of bradyarrhythmia in COVID-19 in excess of 8%[1,2] and have identified these arrhythmias as a significant cause of mortality.[2] Analyses of arrhythmias associated with COVID-19 were conducted early in the pandemic, before mutations were apparent and when medications such as azithromycin were used. Less is known about the risk factors and implications for bradyarrhythmias necessitating pacing in COVID-19 in contemporary practice. We aimed to characterize outcomes in COVID-19 patients who required either temporary or permanent pacing.

We evaluated hospitalized patients diagnosed with COVID-19 in the American Heart Association (AHA) COVID-19 CVD (Cardiovascular Disease) Registry powered by Get With The Guidelines database from December 13, 2019 to April 29, 2021 who developed bradyarrhythmias. Patients within the database are at least 18 years of age and hospitalized for COVID-19 confirmed by reverse transcription polymerase chain reaction, immunoglobulin M (IgM) antibody, or a clinical diagnosis using hospital-specific criteria. We evaluated all patients in the database who received a permanent or temporary pacemaker. We analyzed troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP), C-reactive protein (CRP), d-dimer, and procalcitonin. Cutoffs for elevated values were: troponin >45 ng/L, procalcitonin >1.0 ng/mL, CRP >50 mg/L, d-dimer >230 ng FEU/mL, and standardized, age-adjusted NT-proBNP cutoffs (aged <55 years: 450 pg/mL, aged 55-75 years: 900 pg/mL, aged >75 years: 1.800 pg/mL). We also analyzed patients admitted to the intensive care unit (ICU). Descriptive statistics were reported as mean ± SD, or counts and percentages as indicated. Pearson's chi-square tests and Kruskal tests were used to assess differences between groups. Analyses were performed with RStudio software v3.4.1 on the AHA's Precision Medicine Platform.[4] This project was reviewed by the institutional review committee for the AHA and determined to satisfy a quality improvement exemption.

From December 13, 2019 to April 29, 2021, 44 patients of 32,636 patients hospitalized with COVID-19 (0.13%) developed bradyarrhythmias requiring pacing. These patients were more commonly men (66%), with an average age of 67 years. Patients requiring pacing had a higher percentage of smoking, heart failure, chronic kidney disease, and history of arrhythmias. There was an equal distribution of CVD, diabetes, and hypertension in the nonpacemaker and pacemaker groups (**Table 1**). Inflammatory markers were frequently elevated in patients who required pacing. In terms of electrocardiogram abnormalities, QTc prolongation and atrial fibrillation were prevalent in patients with pacemaker-dependent bradyarrhythmias. Intubation, ICU admission, and shock were more common in patients with bradyarrhythmias requiring pacing. In-hospital mortality occurred in 29.5% of patients with pacing and 14.5% of patients without pacing. Cardiac arrest was common in patients with bradyarrhythmias requiring pacing, occurring in 27% of these patients.

Of the 9,792 patients admitted to an ICU, 31 (0.31%) developed bradyarrhythmias requiring pacemaker placement. These patients with were more likely to have elevated troponin and CRP. Although intubation was similar to other patients admitted to the ICU with COVID-19 (roughly 54%), new-onset heart failure, myocarditis, cardiac arrest, and acute myocardial infarction were higher in patients needing pacing.

Our study is to our knowledge the largest comprehensive analysis to date performed in a national sample evaluating the incidence and implications of bradyarrhythmias requiring pacing in

TABLE 1 Baseline Characteristics and Metrics of COVID-19 Illness Severity

	Patients With HB	Patients Without HB	P Value
Demographics			
Prevalence, %	44 (0.13)	32,333 (99.1)	<0.01
Sex, female	15 (34.1)	14,913 (46)	0.15
Average age, y	67 ± 17.3	62 ± 17.9	0.06
Body mass index	30.2 ± 9.38	31.3 ± 8.45	0.54
Race			
Hispanic	6 (13.6)	6,943 (21.4)	0.28
Non-Hispanic Black	7 (15.9)	7,418 (22.9)	0.06
Non-Hispanic White	31 (70.5)	14,906 (46.1)	-
Past medical history			
Hypertension	31 (70.5)	19,480 (60.2)	0.22
Diabetes mellitus	19 (43.2)	11,553 (35.7)	0.38
Heart failure	17 (38.6)	4,024 (12.4)	<0.01
Dyslipidemia	20 (45.5)	11,718 (36.2)	0.27
Cardiovascular disease[a]	10 (22.7)	7,282 (22.5)	1.00
CKD/hemodialysis	20 (45.5)	5,508 (17.0)	<0.01
Atrial flutter or fibrillation	14 (31.8)	3,612 (11.2)	<0.01
Home medications			
Beta-blocker	16 (36.4)	8,880 (27.5)	0.72
Calcium channel blocker	9 (20.5)	6,769 (27.5)	0.55
ECG findings			
Any ECG abnormality			0.56
Left bundle branch block	3 (6.81)	660 (2.04)	
Right bundle branch block	14 (31.8)	2,022 (6.25)	
QTc prolongation	21 (47.7)	9,675 (29.9)	0.02
Atrial fibrillation	15 (34.1)	2,889 (8.93)	<0.01
Sustained ventricular tachycardia	9 (20.5)	339 (1.05)	<0.01
Inflammatory markers			
Elevated NT-proBNP	10 (22.7)	2,073 (6.41)	<0.01
Missing NT-proBNP	31 (70.5)	25,121 (77.7)	
Elevated troponin	19 (43.2)	5,146 (15.9)	<0.01
Missing troponin	5 (11.4)	11,723 (36.3)	
Elevated CRP	16 (36.4)	10,007 (30.9)	0.24
Missing CRP	21 (47.7)	14,167 (43.8)	
Elevated D-dimer	16 (30)	13,091 (40.5)	1.00
Missing D-dimer	27 (61.3)	18,222 (56.4)	
Hospitalization events			
Intubation	18 (40.9)	5,626 (17.4)	<0.01
ICU-level care	31 (70.5)	9,742 (30.1)	<0.01
Shock	15 (34.1)	3,458 (10.7)	<0.01
Cardiogenic	6 (13.6)	194 (0.6)	
Distributive	3 (6.81)	2,546 (7.87)	
Mixed	6 (13.6)	298 (0.92)	
CRRT	9 (20.5)	1,135 (3.51)	
Cardiac arrest	12 (27.3)	1,350 (4.18)	<0.01
Acute myocardial infarction	6 (13.6)	1,069 (3.31)	<0.01
New-onset heart failure	9 (20.5)	564 (1.74)	<0.01
Myocarditis	2 (4.55)	81 (0.25)	<0.01
VA ECMO	1 (2.27)	9 (0.03)	0.04
Pulseless rhythm			<0.01
Asystole	4 (9.09)	422 (1.31)	
PEA	4 (9.09)	539 (1.67)	
VF/VT	3 (6.81)	106 (0.33)	
Unknown/not documented	1 (2.27)	253 (0.78)	

Continued in the next column

TABLE 1 Continued

	Patients With HB	Patients Without HB	P Value
Outcomes			
In-hospital mortality	13 (29.5)	4,703(14.5)	<0.01
ICU subgroup	31 (70.5)	9,742 (30.1)	
Inflammatory markers			
Elevated troponin	16 (51.6)	2,225 (22.8)	0.02
Missing troponin	2 (6.45)	3,114 (32.0)	
Elevated CRP	14 (45.2)	3,769 (38.7)	0.48
Missing CRP	13 (41.9)	4,126 (42.3)	
Elevated D-dimer	10 (32.3)	4,404 (45.2)	1.00
Missing D-dimer	20 (64.5)	5,034 (51.7)	
Select outcomes			
Intubation	17 (54.8)	5,352 (54.9)	1.00
Shock			<0.01
Cardiogenic	5 (16.1)	181 (1.86)	
Distributive	3 (9.68)	2,395 (24.6)	
Mixed	6 (19.4)	291 (2.99)	
CRRT	9 (29.0)	1,046 (10.7)	<0.01
Cardiac arrest	10 (32.3)	1,093 (11.2)	<0.01
Acute myocardial infarction	5 (16.1)	675 (6.93)	0.10
New-onset heart failure	6 (19.4)	352 (3.61)	<0.01
Myocarditis	2 (6.45)	51 (0.52)	<0.01
VA ECMO	1 (3.23)	9 (0.09)	0.03
Pulseless rhythm			<0.01
Asystole	3 (9.68)	323 (3.32)	
PEA	3 (9.68)	479 (4.92)	
VF/VT	3 (9.68)	99 (1.02)	
Unknown/not documented	1 (3.23)	165 (1.69)	

Values are n (%) or mean ± SD. [a]Cardiovascular disease includes any history of coronary artery disease, percutaneous coronary intervention, myocardial infarction, or coronary artery bypass graft.

CKD = chronic kidney disease; CRP = C-reactive protein; CRRT = continuous renal replacement therapy; ECG = electrocardiographic; HB = heart block or other bradyarrhythmia; ICU = intensive care unit; NT-proBNP = N-terminal pro-B-type natriuretic peptide; PEA = pulseless electrical activity; VA ECMO = venoarterial extracorporeal membrane oxygenation; VF = ventricular fibrillation; VT = ventricular tachycardia.

COVID-19. We found that COVID-19 requiring pacing is a rare complication, and other electrocardiographic abnormalities were prevalent in patients requiring pacing. Biomarkers of myocardial injury are commonly elevated in patients with and without pacemaker-dependent bradyarrhythmias, but the degree of myocardial injury is greater in patients with a need for pacing. Similar to other analyses,[3] patients with bradyarrhythmias requiring pacing exhibited severe systemic illness reflected by high rates of intubation, need for ICU-level care, shock, and cardiac arrest, but the small sample size precludes meaningful comparisons. Previous studies have identified an association between pneumonia and cardiac arrhythmias,[5] but COVID-19 patients with bradyarrhythmias experience poor cardiac outcomes

at uniquely high rates. Though rare, clinicians should be aware of bradyarrhythmias as a manifestation of severe COVID-19 and the association with significant cardiac complications.

Our study has several limitations. First, arrhythmias requiring pacing were rare entities in COVID-19, which limits generalization of findings. Additionally, small number of cases, observational nature of the data, and broad definition of bradyarrhythmias and inability to distinguish permanent or temporary pacing limited comparison of patients with and without pacing needs. However, our study derives strength from analyzing a diverse, nation-wide cohort across multiple time points in the pandemic. Approximately one-half of the patients who developed bradyarrhythmias requiring pacing required ICU-level care, indicating that these rhythms in COVID-19 carry a poor prognosis. Further investigation is needed to understand whether bradyarrhythmias are sequelae of critical illness or direct myocardial involvement by SARS-CoV2.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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