#### ELECTROPHYSIOLOGY

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# New-onset atrial arrhythmias associated with mortality in black and white patients hospitalized with COVID-19

Lilas Dagher MD<sup>1</sup> Hanyuan Shi MD<sup>2</sup> Kan Zhao MD<sup>1</sup> Andrew Wetherbie MD<sup>2</sup> Erik Johnsen MD<sup>2</sup> Deep Sangani MD<sup>2</sup> Saihariharan Nedunchezhian BS<sup>1</sup> Margo Brown BS<sup>1</sup> Peter Miller BS<sup>1</sup> John Schieffelin MD<sup>4</sup> Nassir Marrouche MD<sup>1</sup>

<sup>1</sup> Heart and Vascular Institute, Tulane University School of Medicine, New Orleans, Louisiana, USA

<sup>2</sup> Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana, USA

<sup>3</sup> Section of Pulmonary Diseases, Critical Care, and Environmental Medicine, Tulane University School of Medicine, New Orleans, Louisiana, USA

<sup>4</sup> Department of Pediatrics, Tulane University School of Medicine, New Orleans, Louisiana, USA

#### Correspondence:

Nassir F. Marrouche, MD, Tulane Research Innovation for Arrhythmia Discoveries (TRIAD), Tulane University School of Medicine, Cardiac Electrophysiology, 1430 Tulane Avenue, Box 8548, New Orleans, LA 70112, USA.

Email:nmarrouche@tulane.edu

#### Abstract

**Background:** Specific details about cardiovascular complications, especially arrhythmias, related to the coronavirus disease of 2019 (COVID-19) are not well described. **Objective:** We sought to evaluate the incidence and predictive factors of cardiovascular complications and new-onset arrhythmias in Black and White hospitalized COVID-19 patients and determine the impact of new-onset arrhythmia on outcomes.

**Methods:** We collected and analyzed baseline demographic and clinical data from COVID-19 patients hospitalized at the Tulane Medical Center in New Orleans, Louisiana, between March 1 and May 1, 2020.

**Results:** Among 310 hospitalized COVID-19 patients, the mean age was  $61.4 \pm 16.5$  years, with 58,7% females, and 67% Black patients. Black patients were more likely to be younger, have diabetes and obesity. The incidence of cardiac complications was 20%, with 9% of patients having new-onset arrhythmia. There was no significant difference in cardiovascular outcomes between Black and White patients. A multivariate analysis determined age  $\geq$ 60 years to be a predictor of new-onset arrhythmia (OR = 7.36, 95% CI [1.95;27.76], *p* = .003). D-dimer levels positively correlated with cardiac and new-onset arrhythmic event. New onset atrial arrhythmias predicted in-hospital mortality (OR = 2.99 95% CI [1.35;6.63], *p* = .007), a longer intensive care unit length of stay (mean of 6.14 days, 95% CI [2.51;9.77], *p* = .001) and mechanical ventilation duration(mean of 9.08 days, 95% CI [3.75;14.40], *p* = .001).

**Conclusion:** Our results indicate that new onset atrial arrhythmias are commonly encountered in COVID-19 patients and can predict in-hospital mortality. Early elevation in D-dimer in COVID-19 patients is a significant predictor of new onset arrhythmias. Our finding suggest continuous rhythm monitoring should be adopted in this patient population during hospitalization to better risk stratify hospitalized patients and prompt earlier intervention.

#### KEYWORDS

atrial arrhythmia, cardiac complications, coronavirus disease 2019, d-dimer, mortality

#### 1 | BACKGROUND

In the face of the global pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS- Cov2) virus, a large body of evidence points toward a significant impact of the virus on the cardiovascular system.<sup>1,2</sup> The reported rates of myocardial injury among Coronavirus Infectious Disease of 2019 (COVID-19) patients, defined by an abnormal level of troponin, varied between 10% and 28%.<sup>3,4</sup> Many reports demonstrated myocarditis<sup>5</sup> and heart failure events associated with COVID-19. One of the first studies to report the rate of arrhythmias includes 138 COVID-19 hospitalized patients from Wuhan and shows an incidence of 16.7% in their cohort.<sup>6</sup> Although arrhythmic complications have already been reported in several studies, details regarding the type of arrhythmia and its impact on hospitalization outcomes remain scarce. Additionally, based on our current knowledge, there is no data in the literature that defines predictive factors of cardiac complications and new-onset arrhythmias in COVID-19 hospitalized patients. This data is particularly lacking in the Black population, despite being a community who has been disproportionately affected by COVID-19.<sup>1</sup> Indeed, as of May 2020, the Louisiana Department of Health's database shows that almost 70% of SARS-CoV-2 related deaths are Black patients, despite comprising only 32% of the total state population.<sup>7</sup>

In this study, we sought to characterize cardiovascular and arrhythmic complications in COVID-19 hospitalized patients in New Orleans stratified by race groups, define predictive factors for cardiac and arrhythmic complications during COVID-19 hospitalization, and determine the impact of new-onset atrial arrhythmias on hospitalization outcomes.

#### 2 | METHODS

#### 2.1 Study design and participants

This retrospective observational study was conducted using medical records of patients hospitalized for COVID-19 at Tulane Medical Center in New Orleans, Louisiana, United States, between March 1, 2020 and May 1, 2020, and who were either treated and discharged or died during hospitalization. All patients had confirmed SARS-CoV-2 infection by positive polymerase chain reaction of a nasopharyngeal swab testing in accordance with CDC guidelines. This study was approved by the institutional ethics board of Tulane University School of Medicine (no. 2020–463). Given the retrospective and de identified nature of the data in this study, informed consent was waived.

#### 2.2 Data collection

Demographic and clinical information were collected on admission and during hospitalization by attending physicians. Electronic medical records of the patients were reviewed by a trained team of physicians who worked at the Tulane Medical Center during the pandemic. Demo/II FV

graphics included age, sex, and self-identified race. Comorbid conditions and previous medical history at the time of admission included body mass index (BMI), history of smoking, hypertension, diabetes, and chronic cardiac disease (including coronary artery disease, previous arrhythmia, and congestive heart failure). During hospitalization, we recorded laboratory findings on admission when available, including ferritin, D-dimer, C reactive Protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), absolute lymphocytes count, Btype natriuretic peptide, and troponin. We also collected treatment measures (antiviral, antibiotic, corticosteroid therapies, immune glucocorticoid therapy, and respiratory support), cardiovascular complications, and outcomes during hospitalization.

#### 2.3 | Outcome and predictive factors

Primary endpoints were cardiovascular complications and the incidence of new-onset arrhythmias. Cardiac complications included new onset arrythmias, myocardial infarction, and congestive heart failure. New-onset arrhythmias were defined as the occurrence of arrhythmias (including atrial fibrillation (AF) or flutter, supraventricular tachycardias, bradycardias, or other ventricular arrhythmias not leading to death) in patients with no previous history of arrhythmia at baseline, and detected at presentation or during hospitalization using electrocardiogram (ECG) or telemetry, reviewed by a trained physician for diagnosis confirmation. Myocardial infarction was defined as a significant change in troponin level with signs of myocardial ischemic injury. Vascular complications included ischemic stroke, deep venous thrombosis, and pulmonary embolism. Variables considered for analysis as predictive factors included demographics [age, sex, race], BMI, history of chronic cardiac disease, hypertension, diabetes, smoking status, home medication use (angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB) and aspirin). Another predictive model included a subset of patients with relevant laboratory results (ferritin, D-dimer, CRP, ALT/AST, and absolute lymphocytes count).

#### 2.4 | Statistical analysis

All data were included as study variables to characterize hospitalized patients. Baseline characteristics were compared between Black and White patients using chi-squared, Student's t, Fisher's exact, or Mann-Whitney U-test. This also included differences in admission laboratory results. We then calculated the incidence of cardiovascular complications and new-onset arrhythmias. In the first predictive model, we used logistic regression to evaluate the association between selected base-line clinical characteristics including age, BMI, sex, race, smoking history, hypertension, diabetes, on ACEI-ARB, aspirin, chronic cardiac disease. In the second predictive model including a subset of patients with relevant laboratory testing, we used logistic regression to evaluate the predictive value of serum biomarkers. In exploratory analyses, we also used logistic regression analysis to evaluate the association between

new-onset arrhythmias with in-hospital mortality, ICU length of stay, and intubation duration. Wald tests were used to determine the significance of logistic regression predictors, while t-tests were used for linear regression predictors. SAS, version 9.4 (SAS Institute, Cary, NC) was used for these analyses, and *p*-value of < .05 was considered statistically significant.

#### 3 | RESULTS

#### 3.1 | Baseline characteristics

Three-hundred ten patients were admitted for a COVID-19 infection and either discharged or died after hospitalization from March 1, 2020 to May 1, 2020 in our center. Baseline characteristics of the overall population, as well as stratified by race, are shown in Table 1. For the overall population, mean age was  $61.4 \pm 16.5$  years, including 41.3%(128) males. The most common underlying comorbidities in hospitalized COVID-19 patients included obesity (52.1% of patients), defined by a BMI  $\geq$ 30 kg/m<sup>2</sup>, hypertension (74.8%), and diabetes (44.5%). Thirty percent of patients had a history of chronic cardiac disease. Home medications included ACEI/ARB use in 46.5% of patients, and aspirin in 31.3%.

Black patients constituted the largest majority of COVID-19 hospitalized patients in our cohort (67.1% vs. 12% White patients). At baseline and compared to White patients, hospitalized Black patients were younger (59.6  $\pm$  15.5 years old vs. 69.2  $\pm$  19.5 years old, *p* = .006), had more obesity (15 (39.5%) vs. 119 (57.2%), *p* = .043), were more likely to have diabetes (10 (26.3%) vs. 109 (52.4%), *p* = .003), and were more likely to take ACEI/ARBs (11 (29.7%) vs. 105 (51.5%). *p* = .014). White patients were more likely to have a history of arrhythmia (9 (23.7%) vs. 16 (7.7%), *p* = .007). There were no significant difference in terms of sex and other comorbidities, including a history of hypertension and chronic cardiac diseases, among both race groups.

Regarding the laboratory profile at presentation, black patients had higher CRP (mean of  $5.6 \pm 5.2$  mg/dL vs.  $10.6 \pm 15.5$  mg/dL, p = .001). On the other hand, White patients were more likely to have abnormal NT-proBNP levels on admission compared to Black patients (39.5% of White patients vs. 23.6% of Black patients, p = .005). No significant difference was observed in ferritin levels, D-dimer, troponin, AST, ALT, troponin, and absolute lymphocyte values between both groups (Table 1).

#### 3.2 | Cardiovascular complications

Overall, 62 (20%) COVID-19 hospitalized patients suffered from cardiac complications (Table 2). The most frequent cardiac complication was new-onset arrhythmia (incidence of 9%) with a majority (7.4%) consisting of atrial arrhythmias (AF/atrial flutter). Three patients (1.1%) experienced an atrioventricular block. Only one patient had an atrioventricular nodal reentry tachycardia, and another one had a ventricular tachycardia. Around 5% of patients developed congestive heart failure, and 4% suffered from a myocardial infarction. Among patients who developed new-onset arrhythmia, 15 (53%) patients had a history of congestive heart failure at baseline. Moreover, 10% of total patients experienced a vascular complication, including 6.1% deep venous thrombosis (19), 3.6% pulmonary embolism (11), and 2.3% ischemic cerebrovascular accident (7). There was no difference in the incidence of cardiovascular complications and new-onset arrhythmia between Black and White patients (Table 2).

#### 3.3 | Hospitalization outcomes

In terms of hospitalization outcomes, 257 (83.7%) COVID-19 patients were discharged, and 50 patients (16.3%) died. Around 35% of patients were admitted to the ICU, with an average duration of 7.7 days  $\pm$  7.8. Forty-seven (15.2%) of patients were intubated with a mean total intubation duration of 8.0  $\pm$  8.5 days. Despite a higher comorbidity rate in Black patients, there was no significant difference in mortality, ICU admission, and intubation rates between Black and White patients. The most common cause of mortality was acute respiratory failure due to COVID-19, while cardiac complications were recorded to be the cause of death in 8 (16%) patients.

#### 3.4 | Predictive factors of cardiac complications

In a multivariate analysis including 10 baseline variables (age, sex, race, BMI, smoking status, history of hypertension, diabetes, ACEI/ARB use, aspirin use, and chronic cardiac disease), age was a significant predictor of cardiac complications, as patients older than 60 years were three times more likely to have cardiac complications (OR = 2.99, 95% CI [1.27;7.06], p = .012, Figure 1A), and seven times more likely to suffer from new-onset arrhythmia (OR = 7.36, 95% CI [1.95;27.76], p = .003, Figure 1B). Additionally, patients with a history of chronic cardiac disease have almost five times the risk of developing a cardiac complication during their COVID-19 hospitalization compared to patients without a history of cardiac disease (OR = 4.91, 95% CI [2.35;10.26], p < .001). However, a history of chronic cardiac disease was not predictive of new-onset arrhythmia in this cohort. A history of hypertension was also predictive of cardiac complications (OR = 6.68, 95%CI [1.40;31.86], p = .017, Figure 1A). Sex, race, and diabetes were not associated with cardiac and arrhythmic outcomes in hospitalized COVID-19 patients. Previous ACEI/ARB use was not associated with worse cardiac outcomes.

In an exploratory model including laboratory results (ferritin, D-dimers, AST/ALT, CRP, and absolute lymphocyte count), only D-dimer was found to be a significant predictor of cardiac complications and new-onset arrhythmia among hospitalized COVID-19 patients (OR = 1.049, CI[1.008; 1.090], p = .017 and OR = 1.065 CI[1.015; 1.119], p = .011, respectively).

 TABLE 1
 Demographics, medical history, and laboratory findings at presentation in hospitalized COVID-19 patients, stratified by race groups

Variables	Total (n = 310)	White(n = 38)	Black(n = 208)	p
Demographics				
Age, years (SD)	61.4 (16.5)	69.2 (19.5)	59.6 (15.5)	.006*
Age ≥ 60, n (%)	176 (56.8)	30 (78.9)	30 (78.9) 106 (51.0)	
BMI, kg/m <sup>2</sup> (SD)	35.3 (56.1)	28.0 (7.4)	28.0 (7.4) 37.8 (68.0)	
BMI range, kg/m <sup>2</sup>	13.4-1000			
BMI ≥30, n (%)	176 (52.1)	15 (39.5)	119 (57.2)	.043*
Sex, n (%)				
Male	128 (41.3)	20 (52.6)	78 (37.5)	.083
Female	182 (58.7)	18 (47.4)	130 (62.5)	
Race, n (%)				
White	38 (12.3)			
Black	208 (67.1)			
Asian	2 (0.6)			
Other or unknown	62 (20.0)			
Smoking, n (%)				
Current or former smoker	77 (24.9)	10 (26.3)	52 (25.1)	.060
Never smoke	186 (60.2)	19 (50.0)	135 (65.2)	
Unknown	46 (14.9)	9 (23.7)	20 (9.7)	
Medical history				
Hypertension, n (%)	232 (74.8)	25 (65.8)	163 (78.4)	0.105
Diabetes, n (%)	138 (44.5)	10 (26.3)	109 (52.4)	0.003
Chronic cardiac disease, n (%)	93 (30.1)	14 (36.8)	64 (30.8)	0.464
Coronary artery disease	40 (12.9)	8 (21.1)	28 (13.5)	0.243
Heart failure	52 (16.7)	7 (18.4)	34 (16.4)	0.755
Prior MI	11 (3.6)	2 (5.3)	9 (4.3)	0.802
Arrhythmia	31 (10.0)	9 (23.7)	16 (7.7)	0.007*
Prior heart surgery	8 (2.6)	1 (2.6)	6 (2.9)	0.931
Valvular disease	16 (5.2)	2 (5.26)	13 (6.25)	0.812
Home medications				
ACEI/ARB, n (%)	140 (46.5)	11 (29.7)	105 (51.5)	0.014
Aspirin, n (%)	97 (31.3)	8 (21.6)	74 (36.1)	0.077
Lab results				
Ferritin, ng/L (SD)	998.7 (2891.5)	638.7 (766.2)	1134.8 (3461.9)	0.091
D-Dimer, ng/mL (SD)	768.3 (3460.4)	595.6 (1396.4)	597.5 (2467.7)	0.996
CRP, mg/dL (SD)	10.4 (15.7)	5.6 (5.2)	10.6 (15.5)	0.001*
NT-Pro BNP, pg/mL (SD)	4416.5 (15994.0)	3934.6 (6581.0)	4106.3 (17046.2)	0.939
NT-Pro BNP normal, n (%)	75 (51.0)	4 (60.5)	61 (76.4)	0.005*
NT-Pro BNP abnormal, n (%)	72 (49.0)	15 (39.5)	49 (23.6)	
Troponin, ng/mL (SD)	6.0 (24.1)	13.0 (37.2)	2.6 (8.7)	0.266
Troponin < 0.045 ng/mL, n (%)	85 (48.6)	8 (47.1)	63 (51.2)	0.748

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Variables	Total (n = 310)	White(n = 38)	Black(n = 208)	p
Troponin≥0.045 ng/mL, n (%)	90 (51.4)	9 (52.9)	60 (48.8)	
ALT/AST, n (%)				
No abnormality	155 (52.9)	20 (57.1)	102 (51.8)	0.792
level abnormality ALT > 40 U/L or AST > 40 U/L	116 (39.6)	13 (37.1)	79 (40.1)	
liver injury	22 (7.1)	2 (5.7)	16 (8.1)	
Absolute lymphocytes, x10 <sup>3</sup> /UI	1.3 (0.7)	1.2 (0.6)	1.3 (0.7)	0.854

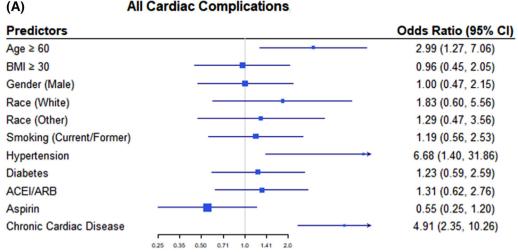
TABLE 2 Incidence of cardiac, arrhythmic, and vascular complications in COVID-19 hospitalized patients, stratified by race groups

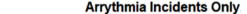
Variables	Total (n = 310)	White (n = 310)	White (n = 310)	White
Cardiac complications, n (%)	62 (20.0)	11 (29.0)	40 (19.2)	0.189
CHF, n (%)	16 (5.2)	4 (10.5)	7 (3.4)	0.081
Myocardial infarction, n (%)	13 (4.2)	1 (2.6)	11 (5.3)	0.452
New-onset arrhythmia, n (%)	28 (9.0)	2 (6.9)	19 (9.9)	0.593
Atrial arrhythmias (AF/Flutter)	23 (7.4)	2 (5.2)	15 (7.2)	0.861
Atrial fibrillation	19 (6.1%)	5 (13.1%)	10 (4.8%)	0.588
Atrial flutter	4 (1.3%)	1 (2.6%)	3 (1,4%)	0.369
Bradycardia or atrioventricular block	3 (1.1)	0	2 (1.0)	0.452
AVNRT	1 (0.4)	0	1 (0.5)	0.595
Ventricular tachycardia	1 (0.4)	0	1 (0.5)	0.595
Vascular complications, n (%)	31 (10.0)	7 (18.4)	22 (10.6)	0.192
DVT or Thromboembolism, n (%)	19 (6.1)	4 (10.5)	13 (6.3)	0.366
Pulmonary embolism, n (%)	11 (3.6)	2 (5.3)	8 (3.9)	0.694
Stroke/cerebrovascular accident, n (%)	7 (2.3)	2 (5.3)	5 (2.4)	0.371

#### 3.5 | New-onset atrial arrhythmias and outcomes

We aimed to investigate the impact of new-onset atrial arrhythmias on hospitalization outcomes. In a multivariate analysis including five variables (age, hypertension, diabetes, history of cardiac disease, and incidence of atrial arrhythmia), the incidence of new-onset atrial arrhythmia was predictive of mortality in COVID-19 hospitalized patients. Patients who experienced new-onset arrhythmias during their hospitalization were almost three times more likely to die (OR = 2.99 95% CI [1.35;6.63], p = .007, Table 3A) than patients who did not. Of note, age was the only other clinical predictor of in-hospital mortality in this multivariate analysis (2.46, 95% CI [1.15;5.24], p = .02, Table 3A). They were also more likely to be admitted to the ICU and had higher risk of intubation. Additionally, their ICU stay duration was significantly longer than patients admitted to the ICU who did not experience new-onset arrhythmias (6.14 days, SE 1.83 95% CI [2.51;9.77], p = .001, Table 3B). They also suffered from longer mechanical ventilation duration (mean of 9.08 days, SE 2.63, 95% CI [3.75;14.40], p = .001).

#### All Cardiac Complications





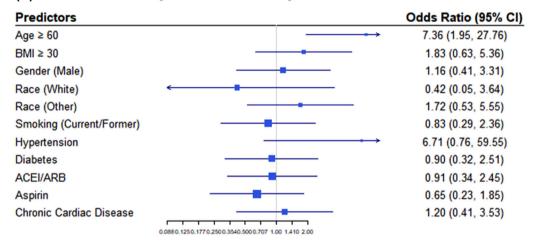


FIGURE 1 Multivariate analysis including demographic and medical history for predictors of cardiac complications (Model A) and new-onset arrhythmia (Model B) [Color figure can be viewed at wileyonlinelibrary.com]

#### DISCUSSION 4

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Our study has three major findings: First, the most common new-onset arrhythmia in COVID-19 patients is AF, with age and D-dimer levels on admission being significant predictors of new-onset arrhythmias in this population. Second, new-onset atrial arrhythmias were predictive of mortality in COVID-19 hospitalized patients and were correlated with longer ICU admissions and intubation duration. Third, despite a higher incidence of comorbidities among Black patients, there was no difference in cardiovascular, arrhythmic, and hospitalization outcomes when compared to White COVID-19 patients.

#### 4.1 Arrhythmias and COVID-19

We demonstrated an incidence of 20% of cardiac complications including 9% new-onset cardiac arrhythmias in hospitalized COVID-19 patients. Atrial arrhythmia (7.4%) including mainly AF(6.1%), was the

most frequently encountered arrhythmia. Only few cases of bradyarrhythmia were found in our cohort. In studies reporting the incidence of unspecified arrhythmia, the rate hovered between 4.3%<sup>8</sup> and 16.7%,<sup>1,6,9</sup> with a marked increase in ICU patients, up to 44%.<sup>6</sup> Few studies reported details regarding the type of arrhythmia encountered. The University of Pennsylvania study<sup>9</sup> which included 700 hospitalized COVID-19 patients, demonstrated a lower rate of new-onset arrhythmic events (7.6%), with 3.5% AF events. Of note, their cohort was younger (mean age  $50 \pm 18$  vs.  $61.4 \pm 16.5$  years) and relatively healthier than ours (hypertension 50% vs. 74% and diabetes 26% vs. 44%). Colon et al.<sup>10</sup> studied 115 COVID-19 hospitalized patients with similar demographic and clinical characteristics to our cohort and reported an incidence of atrial arrhythmias of 16.5%. However, three out of 19 patients who developed an atrial arrhythmia in this study had previous AF,<sup>10</sup> bringing the incidence of new-onset arrhythmia down to 13.9%.

Multiple pathophysiological mechanisms may contribute to the development of arrhythmias in COVID-19 patients.<sup>11</sup> The SARS CoV2 virus has the potential to induce a high inflammatory state with

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#### TABLE 3 Multivariate analysis for predictors of mortality (A) and ICU stay and intubation duration (B)

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A							
Variables	Outcome, death vs. discharge						
	Odds ratios	95% Confidence int	95% Confidence intervals				
Incidence of atrial arrhythmias	2.99	1.35	6.63	.007			
Demographics							
Age $\ge$ 60, n (%)	2.46	1.15	5.24	.020			
Medical history							
Hypertension, n (%)	1.36	0.55	3.37	.513			
Diabetes, n (%)	1.73	0.90	3.32	.100			
Chronic cardiac disease, n (%)	1.16	0.59	2.28	.678			

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Variables	ICU Stay (days)			Intubation du	Intubation duration (days)			
	Coefficient	Standard error	95% Confidence intervals	р	Coefficient	Standard error	95% Confidence intervals	р
Incidence of atrial arrhythmias	6.14	1.83	2.51	9.77	0.001	9.08	2.63	3.75
Demographics								
Age ≥60, n (%)	-0.80	1.88	-4.53	2.93	0.672	-1.40	2.75	-6.96
Medical histories								
Hypertension, n (%)	0.88	2.45	-3.99	5.74	0.721	-0.23	3.72	-7.75
Diabetes complications, n (%)	-1.17	1.63	-4.42	2.07	0.474	-3.09	2.41	-7.97
Chronic cardiac disease, n (%)	-1.10	1.77	-4.62	2.43	0.538	0.14	2.65	-5.23

a massive release of cytokines that can promote arrhythmogenic pathways.<sup>12</sup> Also, in the state of hyperinflammatory response, coronary atherosclerotic plaques are prone to rupture leading to acute cardiac injury and increased susceptibility for arrhythmias. Another possibility is related to a direct viral injury to the myocardium mimicking the presentation of viral myocarditis, as the virus has been consistently detected within myocardial cells.<sup>13,14</sup> A variety of the abovementioned pathophysiological pathways associated with the COVID-19 infection could explain the notable incidence of new-onset arrhythmias.

### 4.2 | Predictive factors of cardiac and arrhythmic complications

In our regression model, an age of 60 years or older was a significant predictor of cardiac outcomes and new-onset arrhythmias. The association between age and COVID-19 hospitalization and cardiovascular outcomes has been proven across multiple studies. Our finding confirm previously published data from both Bhatla et al.<sup>9</sup> and Colon et al.,<sup>10</sup> as both studies found age to be associated with the incidence of cardiac

arrhythmia. In the University of Pennsylvania study,<sup>9</sup> after multivariate adjustment, only age (OR 1.05) and heart failure (OR 5.61) were independently associated with incident AF. We also confirmed the lack of association with sex, race, BMI, diabetes, and hypertension.<sup>9</sup> Moreover, in our cohort, the presence of previous cardiac disease was not predictive of new-onset arrhythmia, which highlights the role of the virus and its accompanying high inflammatory burden in inducing cardiac electrical remodeling regardless of previous underlying disease.

In our population, abnormal D-dimer at presentation was associated with higher odds of developing cardiac complications and newonset arrhythmia in COVID-19 hospitalized patients. The association between D-dimer levels and COVID-19 related outcomes has been consistent in most studies. Increasing D-dimer values have been shown to be predictive of in-hospital mortality.<sup>15-17</sup> While Colon et al.<sup>10</sup> showed higher D-dimer levels in patients who developed arrhythmia, we went further to prove D-dimer level as a predictor of new-onset arrhythmias in a multivariate analysis. D-dimer levels can reflect the severity of the body's response to COVID-19.<sup>16</sup> The high inflammatory state associated with COVID-19 can lead to endothelial injury and to the activation of homeostatic activity,<sup>18</sup> demonstrated by an increase in D-dimer levels. Indeed, D-dimer in COVID-19 patients positively

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correlated with inflammatory markers.<sup>19</sup> Also, D-dimer levels were significantly associated with an increased severity of the COVID-19 infection. All these findings imply that arrhythmic complications in COVID-19 patients are more likely related to the systemic reaction induced by the infection rather than a direct viral injury. Evaluating D-dimer on admission may help select patients in need of close cardiac rhythm monitoring to prompt earlier intervention and possibly lead to better outcomes.

## 4.3 | Impact of new-onset arrhythmias on COVID-19 hospitalization outcomes

New-onset atrial arrhythmia, mainly AF, patients was an independent predictor of increased in-hospital mortality in COVID-19 patients. The development of atrial arrhythmias during hospitalization also increased ICU length of stay and mechanical ventilation days. While we found that atrial arrhythmias increased by almost seven times the risk of mortality, Bhatla et al.<sup>9</sup> showed similar results where incident AF was associated with six times the risk of in-hospital mortality in a univariate analysis, although it did not remain significant after multivariate adjustment. New onset of atrial arrhythmia in this population could be an indicator of a severe inflammatory response induced by the virus, explaining its strong predictive value for inhospital mortality, length of ICU admission and mechanical ventilation. On the other hand, patients who develop atrial arrhythmia would be at higher risk of cardiac decompensation and/or ischemic events, worsening their hospitalization outcomes and prognosis. Thus, we highlight the importance of cardiac rhythm monitoring for further risk stratification.

#### 4.4 Addressing racial differences

Black individuals have been shown to be disproportionately hit by the COVID-19 pandemic. Price-Haywood et al. showed that the black race was associated with 1.96 times the odds of hospital admission compared to the white race.<sup>20</sup> Indeed, 67% of hospitalized patients in our cohort were Black, similar to the percentage reported in the Ochsner study (76.9%). Our registry with 310 total patients in an urban hospital heavily resembled the demographics of the Ochsner study in Louisiana, which featured hospitalized patients that were older (60-70) with a large proportion of Black patients (65% to 75%). In both cases, this rate remains disproportionate given that Black individuals make up 32% of the population of Louisiana. Similarly in the Price-Haywood et al. paper,<sup>20</sup> Black patients had more diabetes and obesity compared to hospitalized White patients. Additionally, Black patients had higher CRP levels at presentation. The higher CRP levels at baseline seen in this population has been observed in previous studies<sup>21,22</sup> and may reflect the underlying chronic inflammatory state associated with a higher comorbidity burden. This observation can partially explain the higher hospitalization rates seen among the Black community, as the underlying chronic inflammation can exacerbate COVID-19 infectious

symptoms. Despite this difference in baseline characteristics. Black patients did not demonstrate worse outcomes compared to White patients, confirming the findings by the Ochsner group and others.<sup>1</sup> In addition, we showed that Black patients were not at higher risk of developing cardiovascular complications and new-onset arrhythmias during hospitalization. Of note, cross-sectional and observational studies have reported lower prevalence and incidence of AF in Black populations, but with a paradoxically higher adverse risk profile and higher risk of stroke.<sup>23</sup> There are no clear evidence as to why this population has less risk of arrhythmia development. We can speculate that while both white and black individuals can develop arrhythmogenic atrial remodeling, the white individual is more susceptible to developing arrhythmias in the setting of the same abnormal tissue substrate. More investigations on the pathophysiology of AF across different demographic and disease profiles would provide insights into this dilemma.

#### 5 | LIMITATIONS

Limitations of this study include that analyses were conducted from a single center serving a large urban population, which may affect generalizability of results. In addition, telemetry was not technically reviewed by the study team, and was up to the discretion of the inpatient teams to classify and identify arrhythmia and complications. Moreover, complete laboratory testing was not performed in all patients. Additionally, a history of cardiac arrhythmia was based on a review of electronic health records, thus previous AF episodes in patients with new-onset AF during hospitalization cannot be definitely ruled out. Finally, the analysis was based on data from electronic medical records, which is subject to entry errors and missing data. Nevertheless, this study provides a comprehensive epidemiologic analysis of hospitalized Black versus White patients as well as it highlights novel findings of the effect of new-onset atrial arrhythmias on mortality and severity of clinical outcomes.

#### 6 CONCLUSION

Cardiac and arrhythmic complications in COVID-19 hospitalized patients are common and do not differ in terms of frequency between White and Black patients, despite a higher comorbidity burden in the latter population. AF was the most frequently encountered arrhythmia. D-dimer level as a marker of COVID-19 severity was predictive of new-onset atrial arrhythmias, reinforcing the concept that arrhythmias are more likely the result of the systemic inflammatory reaction than a direct viral injury to the heart. The fact that new-onset atrial arrhythmia was a predictor of mortality in COVID-19 hospitalized patients emphasizes the importance of inpatient cardiac rhythm monitoring for further risk stratification. Long-term follow-up of COVID-19 patients would be necessary to determine the occurrence or persistence of new-onset arrhythmia beyond hospitalization and after resolution of the infection. The authors declare that there is no conflict of interest.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### ORCID

Lilas Dagher MD <sup>(1)</sup> https://orcid.org/0000-0003-0660-318X Hanyuan Shi MD <sup>(1)</sup> https://orcid.org/0000-0001-6977-6569

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