

RESEARCH LETTER

Arrhythmic Complications of Patients Hospitalized With COVID-19

Incidence, Risk Factors, and Outcomes

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During the course of the coronavirus disease 2019 (COVID-19) pandemic, cardiovascular manifestations have been recognized as an important complication among patients hospitalized with the disease. Arrhythmias have been reported to occur in 7% to 16.7% of hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.^{1,2} However, the incidence of specific types of arrhythmias and its outcomes among patients with COVID-19 have not been well-described. We sought to define the incidence of and risk factors for arrhythmias among patients hospitalized with COVID-19 and to evaluate its association of arrhythmias with outcomes including mortality.

We studied all patients with COVID-19 who were admitted consecutively to New York-Presbyterian/Weill Cornell Medicine and New York-Presbyterian/Lower Manhattan Hospital between March 3 and April 6, 2020. This study was approved by the Weill Cornell Medicine Institutional Review Board. Requirements for informed consent for the study were waived due to the retrospective nature of the study. The data, analytic methods, and study materials that support the findings of this study are available from the corresponding author upon reasonable request. All cases of COVID-19 were confirmed through real-time reverse-transcriptase polymerase chain reaction assays on nasopharyngeal swabs. Using REDCap, patient data were manually abstracted from New York-Presbyterian electronic health records to develop a COVID-19 registry, as previously described.³ Demographics and comorbid conditions were abstracted.

Hypoxia on presentation was defined as use of supplemental oxygen in the emergency department within 3 hours of presentation. Hospitalization events, medication usage, and laboratory values through May 10, 2020, were reviewed.

The primary outcome of the study was 30-day all-cause mortality. Arrhythmias were identified by review of all electrocardiograms and telemetry data obtained during hospitalization. All patients admitted with COVID-19 were placed on telemetry and 82.8% patients underwent at least one ECG. Arrhythmias were defined as atrial fibrillation (AF), atrial flutter, supraventricular tachycardia (VT), frequent premature ventricular contractions (defined as either ≥ 2 premature ventricular contractions on a 6 second 12-lead ECG recording or ≥ 10 premature ventricular contractions per minute on telemetry recording), VT, ventricular fibrillation (VF) and atrioventricular block (second degree or higher). The χ^2 test, Student *t* test, and Wilcoxon rank-sum test were used. Multivariable logistic regression analysis was used to identify predictors of arrhythmias and of 30-day mortality.

A total of 1053 consecutive patients were included in the study analysis. As of May 10, 2020, 723 (68.6%) patients were discharged, 146 (13.9%) were still hospitalized, and 184 (17.5%) had died. The median length of follow-up was 7 (interquartile range [IQR], 3–18; range, 0–62) days. Arrhythmias were identified in 270 (25.6%) of patients. Overall, AF/atrial flutter was identified in 166 (15.8%) patients (with 101 [9.6%] being newly diagnosed). Frequent premature ventricular contractions were

Key Words: atrial fibrillation ■ arrhythmia ■ coronavirus ■ tachycardia

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For Sources of Funding and Disclosures, see page 1231.

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Circulation: Arrhythmia and Electrophysiology is available at www.ahajournals.org/journal/circep

Nonstandard Abbreviations and Acronyms

| | |
|-------------------|---|
| AF | atrial fibrillation |
| aOR | adjusted odds ratio |
| COVID-19 | coronavirus disease 2019 |
| IQR | interquartile range |
| VT | ventricular tachycardia |
| SARS-CoV-2 | severe acute respiratory syndrome coronavirus 2 |
| VF | ventricular fibrillation |

seen in 137 (13.0%) patients. VT or VF was found with 27 (2.6%) patients which included 7 (0.7%) patients with nonsustained VT only, 13 (1.2%) with sustained VT, 9 (0.9%) with polymorphic VT, and 8 (0.8%) with VF. Atrioventricular block (second degree or greater) was seen in 4 (0.4%) patients. The clinical characteristics, imaging findings, and outcomes of the cohort stratified by the presence or absence of arrhythmias are summarized in the Table. Compared with patients without arrhythmias, patients with arrhythmias were older with a higher proportion of males and whites, and significantly more comorbidities. On multivariable regression analysis, age (adjusted odds ratio [aOR], 1.04; $P < 0.001$), male sex (aOR, 2.49; $P < 0.001$), prior history of AF (aOR, 6.03; $P < 0.001$), and hypoxia on presentation (aOR, 2.17; $P < 0.001$) were independently associated with the occurrence of any arrhythmia.

Compared with patients without arrhythmias, patients with arrhythmias more frequently had abnormal chest radiographs. Among 146 (13.9%) patients who underwent echocardiographic imaging, there were no significant differences in left ventricular ejection fraction or proportion of patients with left or right ventricular dysfunction between patients with and without arrhythmias. Overall, compared with patients without arrhythmias, the arrhythmia group had significantly higher peak levels of cardiac troponin I (median, 0.12 [IQR, 0.04–0.56] versus 0 [0–0.05] ng/mL), C-reactive protein (32.1 [18.5–142.4] versus 15.3 [7.1–32] mg/dL), B-type natriuretic peptide (217 [82.5–489.5] versus 41 [16–126] pg/mL), D-dimer (3426 [1677–9676] versus 845 [372–3252] ng/mL), and ferritin (1403 [706–2172] versus 983 [417–1652] ng/mL; $P < 0.001$ for all).

Patients with arrhythmias had significantly more complications during their hospital course including respiratory failure requiring mechanical ventilatory support, hypotension requiring vasopressors, bacteremia, stroke, and venous thromboembolism (Table). There were 13 (1.2%) cardiac arrests due to VT/VF. Among the 745 patients on hydroxychloroquine, 4 (0.54%) had polymorphic VT during their hospital course. Overall in-hospital mortality was significantly greater among patients with arrhythmias compared with those without arrhythmias (34.8% versus 11.5%; $P < 0.001$). Similarly, patients with

AF/atrial flutter and VT/VF had increased mortality when compared with patients without AF/atrial flutter or VT/VF (39.2% versus 13.4%; $P < 0.001$ and 59.3% versus 16.4%; $P < 0.001$, respectively). After adjustment for age, race, and comorbidities, any arrhythmia (aOR, 2.01 [95% CI, 1.34–3.03]) was independently associated with 30-day all-cause mortality.

There are several limitations to the study. This is a retrospective study with data obtained via chart abstraction, which may be subject to error or interpretation. Variations in telemetry monitoring systems across hospital units may have led to possible under-detection of arrhythmias in some cases. Because this study focused on in-hospital outcomes, out-of-hospital deaths following discharge for COVID-19 were not examined.

In this analysis of arrhythmic complications of over 1000 consecutive patients hospitalized with COVID-19, atrial fibrillation/flutter was seen in over 15% of patients with >60% of these occurring in patients without any prior history of AF while VT/VF occurred in <3% of patients. Age, male sex, and hypoxia on presentation were independently associated with the occurrences of arrhythmias. The presence of arrhythmias tracked with markers of disease severity and elevated markers of myocardial injury, inflammation, and fibrinolysis. Although there are likely myriad factors that lead to COVID-19-associated arrhythmias, our findings suggest that arrhythmias may predominantly be a marker of COVID-19 severity. Further studies to elucidate the mechanisms of COVID-19-associated arrhythmias and to assess whether treatments targeting SARS-CoV-2 infection and its associated inflammatory response can reduce arrhythmia occurrence are warranted.

ARTICLE INFORMATION

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Acknowledgments

We thank the following Weill Cornell Medicine medical students for their contributions to the coronavirus disease 2019 (COVID-19) Registry through medical chart abstraction: Zara Adamou, BA, Haneen Aljayyousi, BA, Mark N. Alshak, BA (student leader), Bryan K. Ang, BA, Elena Beideck, BS, Orrin S. Belden, MD/MBA, Anthony F. Blackburn, BS, Joshua W. Bliss, PharmD, Kimberly A. Bogardus, BA, Chelsea D. Boydston, BA, Clare A. Burchenal, MPH, Eric T. Caliendo, BS, John K. Chae, BA, David L. Chang, BS, Frank R. Chen, BS, Kenny Chen, BA, Andrew Cho, PhD, Alice Chung, BA, Alisha N. Dua, MRes, Andrew Eidelberg, BS, Rahmi S. Elahjji, BA, Mahmoud Eljalby, MMSc, Emily R. Erusyal, BS, Kimberly N. Forlenza, MSc, Rana Khan Fowlkes, BA, Rachel L. Friedlander, BA, Gary George, BS, Shannon Glynn, BS, Leora Haber, BA, Janice Havasy, BS, Alex Huang, BA, Hao Huang, BS, Jennifer H. Huang, BS, Sonia Iosim, BS, Mitali Kini, BS, Rohini V. Kopparam, BS, Jerry Y. Lee, BA, Mark Lee, BS, BA, Aretina K. Leung, BA, Han A. Li, BA (student leader), Bethina Liu, AB, Charalambia Louka, BS, Brienne Lubor, BS, Dianne Lumaquin, BS, Matthew L. Magruder, BA, Ruth Moges, MSc, Prithvi M. Mohan, BS, Max F. Morin, BS, Sophie Mou, BA, J. J. Nario, BS, Yuna Oh, BS, Noah Rossen, BA, Emma M. Schatoff, PhD, Pooja D. Shah, BA, Sachin P. Shah, BA, Daniel Skaf, BS, Shoran Tamura, BS, Ahmed Toure, BA, Camila M. Villasante, BA, Gal Wald, BA, Graham T. Wehmeyer, BS (student leader), Samuel Williams, BA, Ashley Wu, BS, Andrew L. Yin, BA, Lisa Zhang, BA.

Sources of Funding

Dr Goyal is supported by American Heart Association grants 18IPA34170185 and 20CDA35310455. This study received support from NewYork-Presbyterian Hospital (NYPH) and Weill Cornell Medical College (WCMC), including the Clinical and Translational Science Center (CTSC; UL1 TR000457) and Joint Clinical Trials Office (JCTO).

Disclosures

Dr Cheung has received consulting fees from Abbott, Biosense Webster, Biotronik and Boston Scientific and fellowship grant support from Abbott, Biosense Webster, Biotronik, Boston Scientific, and Medtronic. Dr Safford has received research grant support from Amgen. The other authors report no conflicts.

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Table. Comparison of Characteristics, Imaging Findings, and Outcomes Stratified by Presence of Arrhythmia

| | All Patients (n=1053) | Arrhythmia (n=270) | No Arrhythmia (n=783) | P Value |
|---|-----------------------|--------------------|-----------------------|---------|
| Clinical Characteristics | | | | |
| Age, y, mean | 62.4±17.3 | 71.1±13.8 | 59.4 ±17.3 | <0.001 |
| Male | 656 (62.3) | 204 (75.6) | 452 (57.7) | <0.001 |
| Body mass index, kg/m ² | 28.5±6.8 | 28.3±6.4 | 28.5±7.1 | 0.778 |
| Race | | | | |
| White | 374 (35.5) | 114 (42.2) | 260 (33.2) | 0.003 |
| Black | 118 (11.2) | 27 (10.0) | 91 (11.6) | |
| Asian | 157 (14.9) | 46 (17.0) | 111 (14.2) | |
| Other | 228 (21.7) | 38(14.1) | 190 (24.3) | |
| Not specified | 176 (16.7) | 45 (16.7) | 131 (16.7) | |
| Coronary artery disease | 157 (14.9) | 74 (27.4) | 83 (10.6) | <0.001 |
| Congestive heart failure | 79 (7.5) | 36 (13.3) | 43 (5.5) | <0.001 |
| Prior history of atrial fibrillation | 94 (8.9) | 68 (25.2) | 26 (3.3) | <0.001 |
| Prior stroke | 73 (6.9) | 26 (9.6) | 47 (6.0) | 0.043 |
| Diabetes mellitus | 313 (29.7) | 92 (34.1) | 221 (28.2) | 0.070 |
| Hypertension | 568 (53.9) | 184 (68.1) | 384 (49.0) | <0.001 |
| Pulmonary disease | 218 (20.7) | 74 (27.4) | 144 (18.4) | 0.002 |
| Renal disease | 97 (9.2) | 36 (13.3) | 61 (7.7) | 0.007 |
| Cirrhosis | 12 (1.1) | 4 (1.5) | 8 (1.0) | 0.515 |
| Active cancer | 64 (6.1) | 19 (7.0) | 45 (5.7) | 0.444 |
| Prior organ transplant | 26 (2.5) | 9 (3.3) | 17 (2.2) | 0.361 |
| Rheumatologic disease | 47 (4.5) | 11 (4.1) | 36 (4.6) | 0.864 |
| Immunosuppressed status | 29 (2.8) | 10 (3.7) | 19 (2.4) | 0.283 |
| Active smoking | 40 (3.8) | 7 (2.6) | 33 (4.2) | 0.229 |
| Baseline medication use | | | | |
| ACE/ARB | 300 (28.5) | 95 (35.2) | 205 (26.2) | 0.005 |
| Statins | 361 (34.2) | 130 (48.1) | 231 (29.5) | <0.001 |
| Hydroxychloroquine | 20 (1.9) | 5 (1.9) | 15 (1.9) | 1.000 |
| Presenting oxygenation | | | | |
| Hypoxia on presentation | 571 (54.2) | 186 (68.9) | 385 (49.2) | <0.001 |
| Radiographic findings | | | | |
| Abnormal chest radiograph n/total n (%) | 877/1036 (84.7) | 244/269 (90.7) | 633/767 (82.5) | 0.001 |
| Bilateral infiltrate | 746/1036 (72.0) | 214/269 (79.6) | 532/767 (69.4) | 0.001 |
| Pleural effusion | 53/1036 (5.1) | 20/269 (7.4) | 33/767 (4.3) | 0.045 |
| Echocardiographic findings | | | | |
| Decreased LVEF <50%, n/total n (%) | 41/146 (28.1) | 26/88 (29.5) | 15/58 (25.9) | 0.628 |

(Continued)

Table. Continued

| | All Patients (n=1053) | Arrhythmia (n=270) | No Arrhythmia (n=783) | P Value |
|--|--------------------------|-----------------------|--------------------------|---------|
| Clinical Characteristics | | | | |
| Lowest LVEF during hospitalization, %, median [IQR] | 59 [48–66] | 61 [47.5–67] | 57.5 [52–66] | 0.690 |
| Decreased RV function, n/total n (%) | 23/146 (15.8) | 15/88 (17.0) | 8/58 (13.8) | 0.598 |
| Clinical outcomes | | | | |
| ICU admission | 349 (33.1) | 178 (65.9) | 171 (21.8) | <0.001 |
| Hypotension requiring vasopressor therapy | 323 (30.7) | 169 (62.8) | 154 (19.7) | <0.001 |
| Respiratory failure requiring mechanical ventilation | 327 (31.1) | 174 (64.4) | 153 (19.5) | <0.001 |
| Bacteremia | 100 (9.5) | 60 (22.2) | 50 (5.1) | <0.001 |
| Venous thromboembolism | 54 (5.1) | 23 (8.5) | 31 (4.0) | 0.003 |
| Stroke/TIA | 18 (1.7) | 16 (5.9) | 2 (0.3) | <0.001 |
| Acute kidney injury requiring new RRT | 34 (3.3) | 12 (4.4) | 22 (2.8) | 0.190 |
| Death | 184 (17.5) | 94 (34.8) | 90 (11.5) | <0.001 |

ACE indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ICU, intensive care unit; IQR, interquartile range; LVEF, left ventricular ejection fraction; RRT, renal replacement therapy; TIA, transient ischemic attack.