RESEARCH LETTER

New-Onset Cardiac Arrhythmias During COVID-19 Hospitalization

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The main manifestation of the coronavirus disease 2019 (COVID-19) is the viral pneumonia, but several manifestations have been also observed in the cardiovascular system. Therefore, a higher risk of cardiac arrhythmias is not unexpected in patients with COVID-19, but data are scant.[1,2]

We investigated the arrhythmic complications in all patients hospitalized for COVID-19 pneumonia at the Intensive Care Unit or the general Medicine Department of our Institution between April 1 and April 26, 2020. This analysis was approved by the Institutional Review Committee, and subjects gave informed consent. The data that support the findings of this study are available from the corresponding author upon reasonable request.

We collected baseline characteristics, laboratory findings, and therapy. All patients were on continuous telemetry during hospitalization. New diagnosis of atrial fibrillation (AF) lasting >30 s, atrial tachycardia lasting >30 s, sustained (>30 s), or nonsustained (>3 beats) ventricular tachycardia and symptomatic bradycardia requiring permanent cardiac pacing that occurred during hospitalization were verified. A daily ECG was also analyzed to measure corrected QT interval (cQT) and evaluate its potential prolongation (cQT>500 ms).

Continuous variables were reported as mean±SD or median (interquartile range). Categorical data were expressed as number (percentage) and proportion of patients reported with the 95% CI. Variables were compared using the Fisher exact or the Mann-Whitney *U* test as appropriate.

The cohort included 30 patients (33% female; mean age 75.2±9.5 years). Baseline characteristics are reported in Table. Three patients (10%) did not undergo any specific pharmacological treatment and 2 (7%) needed only antibiotic therapy. Hydroxychloroquine was largely used (n=25, 83%): alone (n=9, 30%), combined with antiviral drugs (n=14, 46%), or in few cases with antiviral and azithromycin (n=2, 7%). During hospitalization, the mean value of cQT was 454±44 ms. Five cases (17%) of cQT>500 ms were observed, but only in 1 patient (3%), this led to therapy modification.

In 12 patients (40%), we observed new diagnosis of cardiac arrhythmia during hospital stay. Among 22 patients in sinus rhythm at admission, the proportion of new-onset AF was 45% (95% CI, 23%–68%). Episodes of atrial tachycardia were also recorded in 2 patients with AF (9%, 95% CI, 1%–29%). Recurrent nonsustained ventricular tachycardias were also detected in 2 patients without AF (7%, 95% CI, 1%–22%). We did not observe any sustained ventricular tachycardia or symptomatic bradycardia.

Although similar baseline characteristics, patients with new-onset cardiac arrhythmia had higher value of peak white blood cells, higher presence of neutrophils, and higher value of peak CRP (C-reactive protein) and CPK (creatine phosphokinase).

A total of 8 patients (27%) died during hospitalization. Mortality was higher in patients who experienced new-onset cardiac arrhythmia (50% [95% CI, 21%–79%] versus 11%[95% CI, 1%–35%], *P*=0.034). The reason for death was acute respiratory distress syndrome (n=7, 87%), except for one cardiogenic shock in infective endocarditis.

Although myocardial injury and elevation of TnT (troponin T) levels have been observed in some studies during COVID-19 hospitalization, data on the prevalence of

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Nonstandard Abbreviations and Acronyms

ACE	angiotensin-converting enzyme
AF	atrial fibrillation
COVID-19	coronavirus disease 2019
CPK	creatine phosphokinase
cQT	corrected QT interval
CRP	C-reactive protein
TnT	troponin T

cardiac arrhythmias are scant. A study on 138 patients from Wuhan, China, reported that 16.7% of hospitalized and 44.4% of intensive care unit patients with COVID-19 had arrhythmias without further details.[3] Guo et al[4] stratified 187 patients by elevated TnT levels and found more frequent ventricular arrhythmias in the group with high TnT (11.5% versus 5.2%). Kochav et al[2] described case reports of high-grade atrioventricular block, AF onset, and polymorphic ventricular tachycardia. In our registry, 40% of patients developed new-onset arrhythmias during hospitalization. Interestingly, AF was very common with a prevalence of 45% considering patients without AF history. We found that patients with arrhythmias had higher inflammatory markers, such as peak white blood cells, CRP, and CPK, suggesting a more extended inflammatory stress that probably also affected the cardiovascular system. In-hospital mortality was also found significantly higher in these patients (50% versus 11%). With the limited number of patients, our findings should be considered as preliminary observations that need to be confirmed in larger controlled studies.

Many causes should probably call into question: sepsis, neurohormonal and inflammatory stress, fever, abnormal metabolism, hypoxia, anxiety, and concomitant pharmacological therapy.

Patients with cardiovascular disease could particularly suffer the infection due to the imbalance between inflammatory increase and reduced cardiac reserve. More in general, other mechanisms, such as ACE (angiotensin-converting enzyme) 2–related downregulation, cytokine storm, and hypoxemia, could trigger arrhythmias in patients without history of cardiovascular disease.[1]

Side effects of drugs for COVID-19 treatment could also play a role. The use of hydroxychloroquine (or chloroquine), azithromycin, and antiviral drugs could cause prolongation of the QT interval with an increased risk of arrhythmias. We observed cQT prolongation in 5 patients (17%), similar to a previous study,[5] but no sustained ventricular tachycardias were observed.

In our small cohort of consecutive patients hospitalized for COVID-19 pneumonia and continuously monitored using telemetry, new-onset cardiac arrhythmias were frequent, particularly AF. Further studies should focus on COVID-19 arrhythmogenic effects and close heart rhythm monitoring after hospital discharge could be advisable to detect potential silent arrhythmias.

ARTICLE INFORMATION

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Disclosures

D. Giacopelli is employee of BIOTRONIK Italia. The other authors report no conflicts.

REFERENCES

1. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. *J Cardiovasc Electrophysiol.* 2020;31:1003–1008. doi: 10.1111/jce.14479
2. Kochav SM, Coromilas E, Nalbandian A, Ranard LS, Gupta A, Chung MK, Gopinathannair R, Biviano AB, Garan H, Wan EY. Cardiac arrhythmias in COVID-19 infection. *Circ Arrhythm Electrophysiol.* 2020;13:e008719. doi: 10.1161/CIRCEP.120.008719
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020;323:1061–1069.
4. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5:811–818. doi: 10.1001/jamacardio.2020.1017
5. Jain S, Workman V, Ganeshan R, Obasare ER, Burr A, DeBiasi RM, Freeman JV, Akar J, Lampert R, Rosenfeld LE. Enhanced electrocardiographic monitoring of patients with Coronavirus Disease 2019. *Heart Rhythm.* 2020;17:1417–1422.

Table. Patients Characteristics at Hospital Admission, Findings, Therapy, and Outcomes During Hospitalization by Occurrence of New-Onset Cardiac Arrhythmias

Variable	Total (n=30)	No cardiac arrhythmias (n=18)	Cardiac arrhythmias (n=12)	P value
Demographics				
Age, y	75.2±9.5	74.7±10.2	75.9±8.8	0.581
Sex (female), n (%)	10 (33)	8 (44)	2 (17)	0.235
BMI, kg/m²	26.4±4.5	26.5±5.2	26.3±3.6	0.865
Comorbidities, n (%)				
Hypertension	26 (87)	14 (78)	12 (100)	0.130
Diabetes	11 (37)	6 (33)	5 (42)	0.712
Dyslipidaemia	12 (40)	5 (28)	7 (58)	0.136
COPD	6 (20)	3 (17)	3 (25)	0.660
Heart failure	6 (20)	3 (17)	3 (25)	0.660
Persistent atrial fibrillation	8 (27)	7 (39)	1 (8)	0.099
Previous MI	3 (10)	0 (0)	3 (25)	0.054
Previous stroke	4 (13)	2 (11)	2 (17)	1.000
Implanted CIED	4 (13)	2 (11)	2 (17)	1.000
Therapy, n (%)				
ACE inhibitors or ARBs	8 (29)	5 (28)	3 (30)	1.000
Amiodarone	5 (17)	1 (6)	4 (33)	0.128
Magnesium	1 (3)	1 (6)	0 (0)	1.000
Beta-blockers	1 (3)	0 (0)	1 (8)	0.400
Class 1C antiarrhythmic	1 (3)	0 (0)	1 (8)	0.400
Antipsychotics	7 (23)	4 (22)	3 (25)	0.876
COVID-19 therapy, n (%)				
None	3 (10)	2 (11)	1 (8)	1.000
Antibiotic therapy only	2 (7)	1 (6)	1 (8)	1.000
Hydroxychloroquine	25 (83)	15 (83)	10 (83)	1.000
With antiviral	14 (47)	9 (50)	5 (42)	0.722
With antiviral and azithromycin	2 (7)	1 (6)	1 (8)	1.000
Alone	9 (30)	5 (28)	4 (33)	1.000
Monoclonal antibodies	2 (7)	2 (11)	0 (0)	0.503
Low molecular weight Heparins	30 (100)	18 (100)	12 (100)	…
Laboratory findings				
Peak WBCs, cells/µL	12 277±5635	9681±3787	16 171±5830	0.005
Neutrophils at peak WBCs, %	81±13	75±12	90±7	0.001
Lymphocytes at peak WBCs, %	12±11	17±11	6±5	0.005
Minimum WBCs, cells/µL	5959±2154	5727±2259	6305±2031	0.280
Neutrophils at minimum WBC, %	70±15	63±13	79±11	0.002
Lymphocytes at minimum WBC, %	18±10	21±9	13±8	0.023
Peak CRP, mg/L	17 [10–30]	12 [10–28]	18 [15–41]	0.188
Peak PCT, ng/mL	0.4 [0.1–2.5]	0.2 [0.1–0.4]	2.2 [0.7–5.9]	0.023
Creatinine, mg/dL	2.0±1.8	1.3±0.8	3.1±2.4	0.020
Peak CPK, U/L	103 [27–953]	48 [25–158]	953 [51–1984]	0.053
Mean cQT, ms	454±44	452±43	457±46	0.521
cQT >500 ms, n(%)	5 (17)	2 (11)	3 (25)	0.364
Therapy reduction due to QT interval prolongation	1 (3)	1 (6)	0 (0)	1.000
LVEF, %	55 [47–60]	55 [50–60]	50 [40–60]	0.419
Left atrial diameter, mm	41.3±6.9	41.4±7.1	41.0±6.7	0.876

(*Continued*)

Table. Continued

Variable	Total (n=30)	No cardiac arrhythmias (n=18)	Cardiac arrhythmias (n=12)	*P* value
Outcomes, n (%)				
Pericarditis or significant pericardial effusion	0 (0)	0 (0)	0 (0)	…
Myocarditis	0 (0)	0 (0)	0 (0)	…
LVEF reduction	0 (0)	0 (0)	0 (0)	…
Hemodynamic support with inotropic drugs	6 (20)	2 (11)	4 (33)	0.184
Death	8 (27)	2 (11)	6 (50)	0.034

ACE indicates angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; BMI, body mass index; CIED, cardiac implantable electronic device; COPD, Chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CPK, creatine phosphokinase; cQT, corrected QT interval; CRP, C-reactive protein; LVEF, left ventricle ejection fraction; MI, myocardial infarction; PCT, procalcitonin; and WBCs, white blood cells.