RESEARCH LETTER

Electrocardiographic Changes and Arrhythmias in Hospitalized Patients With COVID-19

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) first emerged in Wuhan, China, and subsequently spread globally resulting in the current coronavirus disease-2019 (COVID-19) pandemic.[1] There have been reports of myocardial damage and cardiovascular complications[2]; however, there is limited literature on incidence of cardiac arrhythmias. In this study, we aimed to characterize electrocardiographic characteristics and incidence of arrhythmias in patients admitted with SARS-CoV-2.

Patients ≥18 years old with a confirmed diagnosis of COVID-19 hospitalized at Vidant Medical Center between March 1 to April 26, 2020 were retrospectively identified after Institutional Review Board approval (no. UMCIRB 20-001064 and no. UMCIRB 20-000825). Data on patient demographics, comorbidities, and medications were collected. Baseline, admission, and subsequent serial 12-lead EKGs and telemetry strips were reviewed by 2 independent study investigators to identify rhythm abnormalities and compute baseline and maximum PR interval, QRS duration, and corrected QT interval (QTc) using Bazett formula. In presence of atrial fibrillation, QT measurement was performed using an average of 10 consecutive beats. Differences between mean EKG intervals from admission to maximum value were evaluated using paired t test. Subgroup analysis was performed by gender, race, intensive care unit (ICU) admission, troponin-I levels, and SARS-CoV-2 specific therapy (hydroxychloroquine, azithromycin, tocilizumab). Additional analysis for PR interval was performed in those who received atrioventricular nodal blocking agents (beta-blockers, calcium channel blockers, amiodarone, or digoxin). The data that support findings of this study are available from the corresponding author upon reasonable request.

As of April 26, 2020, there were 107 patients hospitalized with COVID-19. Mean age was 60.0±16.4 years with a predominantly female (58.9%) and Black (69.2%) population. Forty-nine (45.8%) patients required ICU care. Fifty-seven (53.3%) patients were treated with a combination of hydroxychloroquine and azithromycin, 18 (16.8%) patients received only hydroxychloroquine, and 3 (2.8%) patients received only azithromycin. Predominant arrhythmia was sinus tachycardia (30.9%). Tachyarrhythmias were observed in 13 (12.2%) patients. First-degree atrioventricular block was seen in 20 (18.7%) patients and 1 (0.9%) patient developed transient Mobitz II atrioventricular block. There were no cases of torsades de pointes.

PR interval significantly prolonged from 158.7±33.2 ms at the time of admission to 173.9±34.3 ms ($P<0.001$) during hospitalization. Similarly, QRS duration increased significantly from 95.5±21.0 to 99.9±20.1 ms ($P=0.0003$) and QTc increased significantly from 452.0±40.1 to 473.8±45.4 ms ($P<0.001$). PR interval was prolonged regardless of whether patients received atrioventricular nodal blocking agents (Table, last row). Admission and peak PR were longer in Whites (176.4±40.9 versus 185.9±40.1, $P=0.009$) compared to Black (154.1±27.8 versus 170.7±32.2, $P<0.001$). QRS duration significantly increased in ICU patients (95.9±18.4 versus 103.7±18.3, $P<0.001$); but remained unchanged in non-ICU patients ($P=0.34$; Table). Patients had significant lengthening of their QTc intervals during hospitalization regardless of whether they received SARS-CoV-2 specific therapy. PR interval was

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Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019
ICU	intensive care unit
QTc	corrected QT interval
SARS-CoV-2	severe acute respiratory syndrome coronavirus-2

prolonged regardless of the troponin value. QRS duration was increased only in patients with elevated troponin-I (100.7±21.6 to 109.4±21.8 ms, P=0.001; Table).

Ours is the first report of electrocardiographic changes in patients hospitalized with SARS-CoV-2 showing significant prolongation of PR, QRS, and QTc intervals.

PR interval prolonged significantly in all patients admitted with SARS-CoV-2 infection regardless of medication status or troponin elevation. This suggests involvement of cardiac conduction system with SARS-CoV-2 infection which occurs early (ie, before clinically detectable myocardial injury) and is independent of myocardial inflammation. We also observed racial differences in PR intervals, suggesting that Whites may be more susceptible to cardiac conduction system involvement with SARS-CoV-2.

Critically ill patients with SARS-CoV-2 admitted to ICU and those with elevated troponin-I levels had a significantly wider QRS at the time of admission and during the hospital course. We hypothesize that QRS widening is a sign of myocardial injury and may help risk-stratify COVID-19 patients with potential implications with respect to cardiovascular outcomes.

Interestingly, we observed significant QTc lengthening during hospitalization in the small subgroup of patients (n=25) not receiving hydroxychloroquine or azithromycin, suggesting an additional unknown mechanism responsible for QTc prolongation in patients with SARS-CoV-2. Careful monitoring of QTc intervals is warranted, especially in those on hydroxychloroquine or azithromycin.

Our study has several limitations. Ours was a single center, observational, retrospective study of a small population of patients with SARS-CoV-2 without a comparison group. Data was limited to index hospital admission. Follow up data to see whether EKG intervals revert to baseline following recovery from infection are lacking. Approximately 70% of patients in our study received hydroxychloroquine or azithromycin; however, latest data have shown ineffectiveness and possible harm with these drugs in treatment of SARS-CoV-2.[3,4] QRS widening has been previously documented in critically ill ICU patients[5]; hence, this finding may not be specific to SARS-CoV-2. Additional prospective studies with a larger population and longer follow up period are recommended to validate and further elucidate our findings.

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Table. PR Interval, QRS Duration, and QTc Interval (Mean±SD) in Different Subgroups of Patients Hospitalized With COVID-19

EKG Interval	n	Admission Value, ms	Maximum Value, ms	P Value*	n	Admission Value, ms	Maximum Value, ms	P Value*
		ICU				Non-ICU		
PR interval	42	160.7±39.8	179.1±38.3	<0.0001	48	156.9±26.5	169.4±30.1	0.0001
QRS duration	44	95.9±18.4	103.7±18.3	0.0001	51	95.2±23.2	96.6±21.1	0.34
QTc interval	44	460.0±44.3	494.8±48.1	<0.0001	51	445.1±35.0	455.7±34.1	0.004
		Males				Females		
PR interval	34	164.6±38.0	175.5±35.6	0.003	56	155.1±29.7	172.9±33.8	<0.001
QRS duration	37	98.4 ±27.4	105.5±26.4	0.004	58	93.7±15.7	96.2±13.8	0.085
QTc interval	37	444.3±32.2	463.5±37.8	<0.001	58	456.9±44.0	480.4±48.8	<0.001
		Black				White		
PR interval	64	154.1±27.8	170.7±32.2	<0.0001	22	176.4±40.9	185.9±40.1	0.0086
QRS duration	65	94.3±20.4	98.9±19.4	0.005	26	98.5±23.8	102.5±22.8	0.021
QTc interval	65	452.9±39.1	475.2±42.0	<0.0001	26	454.0±44.4	470.4±53.3	0.015
		SARS-CoV-2 specific therapy				No SARS-CoV-2 specific therapy		
PR interval	61	158.9±36.8	159.8±31.8	0.77	21	155.6±26.6	160.1±5.8	0.021
QRS duration	63	96.1±18.2	93.9±16.8	0.21	25	95.0±28.5	100.7±29.2	0.03
QTc interval	63	449.5±41.3	460.5±42.1	0.023	25	453.5±39.5	466.6±49.2	0.006
		Normal troponin-I (<0.04 ng/mL)				Elevated troponin-I (≥0.04 ng/mL)		
PR interval	49	157.2±37.3	170.3±39.1	<0.001	23	161.5±28.2	178.9±28.3	0.0002
QRS duration	49	92.7±17.8	95.2±14.4	0.13	27	100.7±21.6	109.4±21.8	0.0012
		AV nodal blocking agent				No AV nodal blocking agent		
PR interval	50	166.1±35.6	182.8±37.6	<0.001	40	149.4±27.7	162.8±26.1	<0.001

AV indicates atrioventricular; COVID-19, coronavirus disease 2019; ICU, intensive care unit; n, number of pairs; QTc, corrected QT (Bazett formula); and SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

*P value obtained using paired t test.