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The effect of coronavirus infection on QT and QTc intervals of hospitalized patients in Qazvin, Iran

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Abstract

Electrocardiographic (ECG) changes have been investigated in the condition of coronavirus disease (COVID-19) indicating that COVID-19 infection exacerbates arrhythmias and triggers conduction abnormalities. However, the specific type of ECG abnormalities in COVID-19 and their impact on mortality fail to have been fully elucidated. The present retrospective, tertiary care hospital-based cross-sectional study was conducted by reviewing the medical records of all patients diagnosed with COVID-19 infection who were admitted to Booali Sina Hospital in Qazvin, Iran from March to July 2020. Demographic information, length of hospital stay, treatment outcome, and electrocardiographic information (heart rate, QTc interval, arrhythmias, and blocks) were extracted from the medical records of the patients. Finally, a total of 231 patients were enrolled in the study. Atrial fibrillation was a common arrhythmia, and the left anterior fascicular block was a common cardiac conduction defect other than sinus arrhythmia. The deceased patients were significantly older than the recovered ones (71 ± 14 vs. 57 ± 16 years, $p < 0.001$). Longer hospital stay ($p = 0.036$), non-sinus rhythm ($p < 0.001$), bundle and node blocks ($p = 0.002$), ST-T waves changes ($p = 0.003$), and Tachycardia ($p = 0.024$) were significantly prevalent in the deceased group. In baseline ECGs, no significant difference was observed in terms of the absolute size of QT; however, a prolonged QTc in the deceased was about twice of the recovered patients (using Bazett, Sagie, and Fridericia's formula). Serial ECGs are recommended to be taken from all hospitalized patients with COVID-19 due to increased in-hospital mortality in patients with prolonged QTc interval, non-sinus rhythms, ST-T changes, tachycardia, and bundle, and node blocks.

Keywords Arrhythmia · Cardiac · COVID-19 · Long QT syndrome · QTc interval

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1 Introduction

Since the first cases of corona infection were reported at the end of 2019, the SARS-COV-2 virus has rapidly spread worldwide and become a pandemic [1, 2]. In particular, the high rate of transmission has made Coronavirus a serious universal threat to public health. No proven effective treatment is currently found against the virus, and its effect on other diseases such as inherited syndromes is unknown [3]. Studies have indicated that while most patients are asymptomatic or have minor symptoms [4], those with underlying diseases, especially cardiovascular disease or the elderly may have a worse prognosis than others. In addition, understanding that most clinical manifestations are related to the respiratory system is essential, however, the disease may also affect the cardiovascular system [5, 6]. The myocardial injury in COVID-19 may be secondary to systemic inflammatory response syndrome, increased catecholamine, coronary artery thrombosis, and direct invasion of the myocardium by the virus [7, 8].

The high prevalence of arrhythmias in COVID-19 is associated with several factors such as hypoxemia due to acute respiratory distress, acute decrease in cardiac hemodynamics, myocarditis, blunt cardiac injury, acute inflammatory response, direct viral invasion, and/or use of QT prolonging medications [9–12]. Also, investigational treatments for COVID-19 may increase the risk of ventricular arrhythmia through drug interactions. Many articles have reported that COVID-19 infection and related medications increase the QT interval and the risk of arrhythmias [13–15].

Data mining is increasingly used to explore large databases which are necessary to provide timely and accurate decisions, subject to available computer resources, and the temporal ability to understand and act [16]. Healthcare is a crucial field of application of data science, especially in the COVID-19 pandemic since the beginning of 2020 [17]. Rescue and recovery of a patient with COVID-19 can be predicted by analyzing the relationships between parameters such as demographic characteristics (age and gender), clinical symptoms, medical examinations, and paraclinical findings. Using different approaches that may explore the important determinants of mortality due to pneumonia (COVID-19 pneumonia) is important at patient's and hospital levels [18]. The growing emphasis on data mining in medical fields can provide the right environment for change and improvement [19].

The present predictive data mining study aimed to further characterize electrocardiographic (ECG) abnormalities (arrhythmia and cardiac conduction abnormality) in patients with COVID-19 and determine which type of arrhythmias were more common in deceased patients. In particular, the present study focused on the risk of QT interval prolongation which is a serious issue in managing hospitalized patients with COVID-19.

2 Materials and methods

The present retrospective, tertiary care hospital-based cross-sectional study was conducted by reviewing the medical records of all patients diagnosed with COVID-19 infection who were admitted to Booali Sina Hospital in Qazvin, Iran from March

to July 2020. Clinical symptoms of COVID-19 pneumonia include cough, fever, pleurisy, and dyspnea. The inclusion criteria were confirmed cases diagnosed with COVID-19 by chest CT scan and positive Real-Time PCR (cobas® SARS-CoV-2 Test) samples of the nasopharyngeal swab. Patients who were diagnosed with COVID-19 by only clinical symptoms and imaging were excluded from the study. The data were registered and available in the patient files and were reviewed and monitored by various officials.

Demographic information, length of hospital stay, mortality rate, electrocardiographic information including cardiac and sinus arrhythmia (sinus tachycardia and bradycardia), and other rhythms (atrial fibrillation, atrioventricular node block (AV) block, and other non-sinus rhythms), and absolute and heart rate-corrected QT (QTc) interval were collected using the three formulas of Bazett, Fridericia, and Sagie in Lead II and Lead V3. Also, common arrhythmia and cardiac conduction defects (left bundle branch block [LBBB], right bundle branch block [RBBB], left anterior fascicular block [LAHB], left posterior fascicular block [LPFB], premature atrial complex [PAC], and premature ventricular contraction [PVC]) were extracted from the medical records of the patients. All participants had 12 leads of ECG on admission and, some of them had second and third ECGs if they were taken. QT-interval is defined as the time from the beginning of the QRS-complex to the end of the T-wave. Normal QTc intervals are less than 440 ms in men and 460 ms in women [20]. QTc interval greater than 460 ms in men and 480 ms in women was considered a prolonged QTc interval [21].

Statistical analysis was performed using SPSS software (version 25.0). Descriptive statistics including absolute frequency and percentage for qualitative data (nominal and ordinal variables) and mean ± SD for quantitative data were calculated. The student's t-test was used to compare continuous variables between two groups. Chi-squared test was used to investigate the frequency distribution in the agreed tables and Fisher's exact test was used when necessary. A p-value less than 0.05 is statistically significant. The medical record number and confidential information of patients with COVID-19 were deleted to observe the ethical consideration in the present study [22]. The present study was approved by the Ethics Committee of Qazvin University of Medical Sciences, Qazvin, Iran (IR.QUMS.REC.1399.379).

3 Results

A total of 436 patients were hospitalized with positive COVID-19 RT-PCR tests during the study period. Of the studied patients, 321 had a baseline ECG at the time of admission. The summary of baseline demographics information and ECGs data are presented in Tables 1 and 2, respectively. According to the results, the mean age of participants was 60 ± 17 years. Also, the deceased and recovered patients were 71 ± 14 and 57 ± 16 years, respectively which indicated that deceased patients were significantly older than the recovered ones ($P < 0.001$). However, no significant relationship was observed between gender and place of residence in patients. Length of hospital stay was significantly longer in deceased patients ($P = 0.036$).

Table 1 Demographic information of alive and deceased COVID-19 patients in the present study

		Groups			
Demographic Information		Alive N=250 Mean±SD or N (%)	Death N=71 Mean±SD or N (%)	Total N=321 Mean±SD or N (%)	*P* Value
Age (year)		57±16	71±14	60±17	<0.001
Duration of hospitalization (days)		8±7	11±13	8±8	0.036
Sex	Female	121 (48.4)	30 (42.3)	151 (47.0)	0.360
	Male	129 (51.6)	41 (57.7)	170 (53.0)	
Residency	City	168 (67.2)	51 (71.8)	219 (68.2)	0.460
	Village	82 (32.8)	20 (28.2)	102 (31.8)	

Table 2 ECG results of alive and deceased COVID-19 patients in hospital admission

			Groups Mean±SD or N (%)			
ECG Information			Alive N=250	Death N=71	Total N=321	*P* value
Rythm		NSR	164 (65.6)	38 (53.5)	202 (62.9)	0.001
		Atrial fibrillation	6 (2.4)	10 (14.1)	16 (5.0)	
		Sinus tachycardia	67 (26.80	20 (28.2)	87 (27.1)	
		Sinus bradycardia	7 (2.8)	0	7 (2.2)	
		Other	6 (2.4)	3 (3.2)	9 (2.8)	
Cardiac conduction abnormality	with	LBBB	8 (3.2)	5 (7.0)	13 (4.0)	0.002
		LAHB	23 (9.2)	8 (11.3)	31 (9.3)	
		LPHB	1 (0.4)	0	1 (0.3)	
		RBBB	9 (3.6)	4 (5.6)	13 (4.0)	
		PAC & PVC	5 (2.0)	7 (9.8)	12 (3.7)	
		others	17 (6.8)	9 (12.7)	26 (8.1)	
	without		197 (78.8)	43 (60.6)	240 (74.8)	
ST-T changes		No	212 (84.8)	48 (67.6)	260 (81.0)	0.003
		Yes	38 (15.2)	23 (312.4)	61 (19.0)	
QT interval mini box II			9±1	9±1	9±1	0.927
QT interval mini box V3			9±1	10±1	9±1	0.301
QT interval II (msec)			368±47	367±58	368±49	0.927
QT interval V3 (msec)			374±52	381±57	376±53	0.301
QT interval II (msec)			368±47	367±58	368±49	0.927
QT interval V3 (msec)			374±52	381±57	376±53	0.301
Heart rate (/min)			88±19	94±23	89±20	0.024

Normal Sinus Rhythm (NSR), Atrial Fibrillation (AF), Atrioventricular (AV) Block, Left bundle branch block (LBBB), Right bundle branch block (RBBB), Left anterior fascicular block (LAHB), Left posterior hemiblock (LPHB), Premature atrial complex (PAC), Premature ventricular contraction (PVC)

Of these patients, 62.9%, 27.1%, and 10% had sinus rhythm, sinus tachycardia, and other rhythms (atrial fibrillation, sinus bradycardia, AV block, and other non-sinus rhythms), respectively. The non-sinus rhythm was significantly higher in the

Table 3 The second ECG results of alive and deceased COVID-19 patients

			Groups Mean±SD or N (%)			
ECG Information			Alive N=41	Death N=24	Total N=65	*P* value
Rythem		NSR	33 (80.5)	12 (50.0)	45 (69.2)	0.029
		Atrial fibrillation	2 (4.8)	5 (20.8)	7 (10.7)	
		Sinus bradycardia	0	1 (4.2)	1 (1.5)	
		Sinus tachycardia	6 (14.6)	6 (25.0)	12 (18.5)	
Cardiac conduction Abnormality	with	LAHB	4 (9.7)	4 (16.7)	8 (12.3)	0.037
		LBBB	2 (4.9)	2 (8.3)	4 (6.2)	
		RBBB	2 (4.9)	2 (8.3)	4 (6.2)	
		AV Block	2 (4.9)	1 (4.2)	3 (4.6)	
		other	2 (4.9)	5 (20.8)	7 (10.8)	
	without		30 (73.2)	12 (0.5)	42 (64.6)	
ST-T changes		No	30 (73.2)	13 (54.2)	43 (66.2)	0.118
		Yes	11 (26.8)	11 (45.8)	22 (33.8)	
QT interval minibox II			10.0±1.0	10.0±2.0	10.0±1.0	0.734
QT interval minibox V3			10.0±1.0	10.0±1.0	10.0±1.0	0.532
QT interval II (msec)			389±52	384±63	387±56	0.734
QT interval V3 (msec)			393±48	402±60	396±52	0.532
QT interval II (msec)			389±52	384±63	387±55	0.734
QT interval V3 (msec)			393±48	402±60	396±52	0.532
RR interval minibox			19.0±5.0	18.0±5.0	19.0±5.0	0.328
Heart rate (/min)			81.9±19.9	88.5±22.2	84.3±20.9	0.219

*Normal Sinus Rhythm (NSR), Atrial Fibrillation (AF) **atrioventricular (AV) node, Left anterior fascicular block (LAHB), Left bundle branch block (LBBB), Right bundle branch block (RBBB), Premature ventricular contraction (PVC)

deceased group at the time of admission ($P<0.001$). Cardiac conduction abnormalities observed on the ECG include LBBB, RBBB, LAHB, LPHB, PAC, and PVC which were significantly higher in the deceased group ($P=0.002$). Atrial fibrillation was also common besides sinus arrhythmia and left anterior fascicular block was a common cardiac conduction abnormality. About a quarter of patients had ST-T change which was significantly higher in the deceased group ($P=0.003$). The mean heart rate (HR) in deceased patients was significantly higher than that of the recovered group ($P=0.024$).

Among 321 patients with baseline ECGs on admission, 65 patients had a second ECG. The summary of data of the second ECG is presented in Table 3. Examination of ECG data in these individuals indicated that non-sinus rhythm and bundle block (LAHB, LBBB, and RBBB) and AV, PAC, and PVC in the second ECG were significantly prevalent in the deceased group ($P=0.029$ and 0.037, respectively). No statistically significant difference was observed in ST-T change in the two groups.

A third ECG was obtained from 28 patients of the 65 patients with a second ECG. The summary of data of the third ECG is presented in Table 4. Examination of the ECG data in these individuals revealed that the non-sinus rhythm was slightly higher

Table 4 The third ECG results of alive and deceased COVID-19 patients

			Groups Mean±SD or N (%)			
ECG Information			**Alive N=19**	**Death N=9**	**Total N=28**	**P-value**
Rhythm		NSR	17 (89.5)	5 (55.6)	22 (78.6)	0.065
		Atrial fibrillation	0	2 (22.2)	2 (7.1)	
		Sinus bradycardia	1 (5.3)	0	1 (3.6)	
		Sinus tachycardia	1 (5.3)	2 (22.2)	3 (10.7)	
Cardiac conduction Abnormality	With	LAHB	2 (10.5)	3 (27.3)	5 (16.7)	0.167
		LBBB	1 (5.2)	1 (9.0)	2 (6.7)	
		RBBB	1 (5.2)	1 (9.0)	2 (6.7)	
		others	2 (10.5)	2 (18.0)	3 (10.0)	
	Without		14 (73.7)	4 (36.4)	18 (60.0)	
ST-T changes		No	15 (78.9)	3 (33.3)	18 (64.3)	0.019
		Yes	4 (21.1)	6 (66.7)	10 (35.7)	
QT interval minibox II			10.0±2.0	9.0±2.0	10.0±2.0	0.091
QT interval minibox V3			10.0±1.0	9.0±2.0	10.0±1.0	0.111
QT interval II (msec)			416±73	364±85	396±80	0.091
QT interval V3 (msec)			416±40	372±76	401±57	0.111
QT interval II (msec)			419±74	364±85	397±81	0.091
QT interval V3 (msec)			417±41	372±76	401±58	0.111
Heart rate (/min)			77.4±11.5	109.8±40.0	88.9±29.4	0.024

***Normal Sinus Rhythm (NSR), Atrial Fibrillation (AF), Left anterior fascicular block (LAHB), Left bundle branch block (LBBB), Right bundle branch block (RBBB), Premature ventricular contraction (PVC)

in the third ECG of the deceased group. The bundle block and AV and PVC node block were not highly prevalent in the third ECG of the two groups. The presence of ST-T change in the deceased group was significantly higher than that in the recovered group ($P=0.019$). In addition, the HR level in the deceased group was significantly higher than that of the improved group ($P=0.024$).

The QTc interval in leads II and V3 with three QT interval correction methods (the Bazett, Sagie, and Fridericia's formula) of alive and deceased patients with COVID-19 are presented in Table 5. In baseline ECGs, no statistically significant difference was found in absolute QT size between the two groups. However, the QTc interval in the deceased patients was higher than that of the recovered ones ($P<0.001$, 0.1018, and 0.005 using Bazett, Sagie, and Fridericia's formula in lead V3, respectively) and prolonged QTc interval was about twice in the deceased patients than the recovered group. Also, the QT interval in the second and third ECGs was not significantly different between the deceased and recovered groups; however, a statistically significant difference was observed in the QTc interval by the Bazett method in lead V3 ($P=0.025$).

Table 5 QTc interval in lead II and V3 by three correction QT interval methods (the Bazzet, Sagie and Fridericia's formula) of alive and deceased COVID-19 patients

QTc interval prolongation		Groups Mean ± SD or N (%)			
Lead	**Correction QT methods** (1st, 2nd, 3rd)	**Alive**	**Death**	**Total**	**P**
II	B1	53 (21.2)	30 (42.3)	83 (25.9)	0 < 001
		438 ± 40	452 ± 49	441 ± 42	0.021
V3	B1	63 (25.2)	34 (47.9)	97 (30.2)	0 < 001
		445 ± 43	467 ± 50	450 ± 46	< 0.001
II	S1	11 (4.4)	9 (12.7)	20 (6.2)	0.011
		412 ± 34	417 ± 42	413 ± 36	0.253
V3	S1	21 (8.4)	14 (19.7)	35 (10.9)	0.007
		418 ± 39	431 ± 43	421 ± 40	0.018
II	F1	16 (6.4)	11 (15.5)	27 (8.4)	0.015
		413 ± 37	421 ± 47	414 ± 39	0.146
V3	F1	23 (9.2)	15 (21.1)	38 (11.8)	0.006
		420 ± 42	436 ± 47	423 ± 43	0.005
II	B2	13 (31.7)	11 (45.8)	24 (36.9)	0.255
		446.2 ± 49.4	459.2 ± 48.6	450.9 ± 49.1	0.324
V3	B2	17 (41.5)	14 (58.3)	31 (47.7)	0.189
		451.5 ± 39.4	477.9 ± 53.2	461.3 ± 46.4	0.025
II	S2	6 (14.6)	7 (29.2)	13 (20.0)	0.157
		423.5 ± 42.1	428.2 ± 44.6	425.2 ± 42.8	0.684
V3	S2	7 (17.1)	6 (25.0)	13 (20.0)	0.441
		428.3 ± 36.5	444.3 ± 45.3	434.2 ± 40.4	0.125
II	F2	6 (14.6)	7 (29.2)	13 (20.0)	0.157
		425.5 ± 45.8	431.7 ± 48.7	427.8 ± 46.6	0.623
V3	F2	8 (19.5)	8 (33.3)	16 (24.6)	0.212
		430.6 ± 37.9	450.2 ± 49.3	437.8 ± 43.2	0.076
II	B3	6 (31.6)	7 (63.6)	13 (43.3)	0.088
		473.2 ± 67.4	470.3 ± 65.1	472.1 ± 65.4	0.910
V3	B3	8 (42.1)	9 (81.8)	17 (56.7)	0.034
		469.5 ± 39.5	490.9 ± 58.1	476.7 ± 46.6	0.244
II	S3	4 (21.1)	2 (18.2)	6 (20.0)	0.850
		450.5 ± 66.3	424.1 ± 64.1	440.5 ± 65.6	0.303
V3	S3	5 (26.3)	3 (27.3)	8 (26.7)	0.954
		448.0 ± 33.7	435.5 ± 53.2	443.8 ± 40.7	0.435
II	F3	4 (23.5)	2 (18.2)	6 (21.4)	0.736
		452.9 ± 68.0	430.5 ± 68.8	444.4 ± 68.0	0.398
V3	F3	5 (26.3)	4 (36.4)	9 (30.0)	0.563
		450.7 ± 36.3	446.3 ± 57.8	449.2 ± 43.6	0.797

Bazzet (B), Sagie (S) and Fridericia (F)'s formula

4 Discussion

The findings of the present study demonstrated that the mean age of deceased and recovered patients was 71 ± 14 and 57 ± 16 years; therefore, dead patients were significantly older than recovered ones. Other similar studies also have reported a significant relationship between age and patients outcome [23, 24]. Therefore, these findings indicated the need for serious prevention in the elderly and targeted vaccination in this group. No significant relationship was found between gender and place of residence among recovered and deceased patients in this study which is consistent with other studies [25]. At baseline ECGs on admission, the non-sinus rhythm was significantly more prevalent in the deceased group than in the recovered one. Non-sinus rhythm in the patients may indicate the presence of underlying heart disease which is a risk factor for severe disease or recently developed following COVID-19 which in this case is considered a sign of the severity of the disease [26]. Examination of previous medical records (history of heart disease and ECGs] may help to distinguish between the two reasons, unfortunately, our patients had no previous records. A meta-analysis suggested that patients with severe COVID-19 have a higher risk of arrhythmia; therefore, COVID-19 may be a risk factor for arrhythmia which increases as the disease progresses [27].

In a similar study by Antwi-Amoabeng et al. [28], HR in the deceased people was significantly higher than that in the recovered group. This finding may be due to increased sympathetic tone, inflammatory cytokines, febrile agents, hypoxia due to lung involvement, or a secondary reaction to dysfunction of other body systems, including the liver, kidneys, and brain in infected individuals. It also can be an indirect indicator of myocarditis, pericarditis, or isolated dysfunction of the conduction system [12]. The presence of tachycardia can be used as an indicator of disease severity regardless of the cause of high rates in patients. About a quarter of the examined ECGs had ST-T change and were significantly higher in the deceased group. Barman et al. indicated that ST-T changes are closely associated with the severity of COVID-19. ST-T changes can be a symptom of heart disease or direct or indirect impact of the virus through ischemia, myocarditis, or pericarditis [29].

Other observed abnormalities in ECG including LBBB, RBBB, LAHB, LPHB, PAC, and PVC were significantly higher in the deceased group. The presence of abnormalities in the ECG of the patient is an alarm signal of survival outcome and requires eliminating the causes such as electrolyte disorder, ischemia, heart failure, or myocarditis. The results of the study by Zuin et al. demonstrated a higher risk of mortality in COVID-19 patients with LBBB, although they failed to assess whether LBBB existed before COVID-19 infection or occurred due to a cardiac complication or injury [30]. People who have any abnormalities in the primary ECG are required to be closely monitored and followed up.

In general, no statistically significant difference was observed in the absolute size of QT between the two groups; however, the QTc interval was more prolonged in the deceased patients than in the recovered ones after modifying the QT interval using different formulas. QT-interval represents the time of the depolarization and repolarization of the ventricle [31]. QT prolongation is an independent risk factor for stroke, sudden death, and all-cause mortality [32] which often occurs with Torsade de Pointes [33, 34]. These facts indicate that being aware of the information of QT-interval is crucial. This finding suggests that the QTc interval be used instead of the

absolute QT interval to estimate the result [35]. Also, using at least two correction formulas (one organ lead [lead II] and a precordial lead [V3 or V5]) or at least using Bazett's formula is recommended in leads II and V3. The measurement of QT in lead V3 is more accurate than in lead II due to its longer QT interval.

Examination of the second ECG indicated a non-sinus rhythm and bundle blocks including LBBB, RBBB, and LAHB as the first ECG, and node blocks of AV, PAC, and PVC were significantly higher in the deceased group. ST-T change was higher in the second ECG of the deceased group; however, no statistically significant difference was observed in this component between the two groups. Also, the mean HR was slightly higher in the deceased group than in the recovered one which could be due to the small number of second ECGs. Among the examined second ECGs, a significant difference was observed in the QTc interval by Bazett's method in lead V3. Furthermore, QTc intervals were slightly different between the two groups in other modification methods.

Examination of ECG data in 28 patients indicated that only ST-T change and mean HR in the deceased group was significantly more than that in the recovered individuals. Non-sinus rhythm and bundle block and AV and PVC node block were not significantly different in the third ECG of the studied groups. It seems that this difference will be better shown if the number of samples increases. The high incidence of arrhythmias in COVID-19 is according to numerous factors such as hypoxemia, an acute decline in cardiac hemodynamics, myocarditis, cardiac injury, prominent inflammatory response, direct viral invasion, and/or use of QT prolonging medications [12]. Despite hospitalization and treatment of the potentially treatable causes of tachycardia such as fever, associated bacterial infection, and electrolyte disorder, persistent tachycardia may be an important risk factor, which represents the refractory activity of an inflammatory and sympathetic system. Mistry et al. stated in a retrospective analysis that beta-blockers were associated with reduced mortality in critically ill ventilated patients with COVID-19 who developed tachycardia and were treated with norepinephrine [36].

The findings of the present study emphasize the importance of considering ECG abnormality in patients with COVID-19 since abnormally prolonged QTc intervals and serial changes in QT intervals are important components in determining mortality.

Limitations of the present study include the retrospective nature, small number of patients who had second and third ECGs requested by a physician, and heterogeneity of the study sample. A longitudinal study is suggested to perform serial ECG for all patients with Covid-19 which is efficiently and accurately analyzed by having the right number of homogeneous samples [37]. Manually measuring QT-interval is time-consuming, especially for 12-lead ECG. Hence, a smartphone-based automatic QT interval measurement system can assist physicians to assess QT prolongation before and after prescribing a new medication [38] and shorten the time for data collection, and accurately detect QT intervals [39]. Therefore, conducting a study for implementing smartphones in ECG monitoring of patients with COVID-19 is recommended. Also, several medications that prolong the QT interval such as hydroxy-

chloroquine and azithromycin were used for treating COVID-19 infection early in the onset of the pandemic which increased the incidence of torsades de pointes and sudden cardiac death [40–42]. These medications are no longer used in guidelines for preventing and treating COVID-19 due to the risks and lacking efficacy.

In conclusion, the present study highlights cardiac arrhythmias such as AF and AV block during COVID-19 infection and careful considerations of cardiac management in patients. Also, understanding the risk should guide additional safety measures such as monitoring of the corrected QTc interval due to increase in-hospital mortality in patients with prolonged and increasing QTc interval, non-sinus rhythms, ST-T changes, tachycardia, and bundle and node blocks. Therefore, taking a serial ECG from all hospitalized patients with COVID-19 is recommended.

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Declarations

Conflict of interest The authors declared no conflict of interest.

Ethics approval: The ethics committee of the Qazvin University of Medical Sciences approved the present study's protocol with the following ethics code: IR.QUMS.REC.1399.379.

References

1. Lu H, Stratton CW, Tang YW (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol 92(4):401–402
2. Hui DS, Azhar EI, Madani TA, Ntoumi F, Kock R, Dar O, Ippolito G, Mchugh TD, Memish ZA, Drosten C (2020) The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 91:264–266
3. Gao J, Tian Z, Yang X (2020) Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends 14(1):72–73
4. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet 395(10229):1054–1062
5. Kwenandar F, Japar KV, Damay V, Hariyanto TI, Tanaka M, Lugito NPH, Kurniawan A (2020) Coronavirus disease 2019 and cardiovascular system: A narrative review. IJC Heart & Vasculature 29:100557
6. Guo J, Huang Z, Lin L, Lv J (2020) Coronavirus disease 2019 (COVID-19) and cardiovascular disease: a viewpoint on the potential influence of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on onset and severity of severe acute respiratory syndrome coronavirus 2 infection. J Am Heart Assoc 9(7):e016219
7. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, Rabbani L, Brodie D, Jain SS, Kirtane AJ (2020) The variety of cardiovascular presentations of COVID-19. Circulation 141(23):1930–1936
8. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O (2020) Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol 5(7):831–840
9. Wang C, Horby PW, Hayden FG, Gao GF (2020) A novel coronavirus outbreak of global health concern. The lancet 395(10223):470–473
10. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, Brown TS, Der Nigoghossian C, Zidar DA, Haythe J (2020) Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol 75(18):2352–2371

11. Kazi DS, Martin LM, Litmanovich D, Pinto DS, Clerkin KJ, Zimetbaum PJ, Dudzinski DM (2020) Case 18-2020: a 73-year-old man with hypoxemic respiratory failure and cardiac dysfunction. N Engl J Med Overseas Ed 382(24):2354–2364
12. Desai AD, Boursiquot BC, Melki L, Wan EY (2021) Management of arrhythmias associated with COVID-19. Curr Cardiol Rep 23(1):1–9
13. Ramireddy A, Chugh H, Reinier K, Ebinger J, Park E, Thompson M, Cingolani E, Cheng S, Marban E, Albert CM (2020) Experience with hydroxychloroquine and azithromycin in the coronavirus disease 2019 pandemic: implications for QT interval monitoring. J Am Heart Assoc 9(12):e017144
14. Gasperetti A, Biffi M, Duru F, Schiavone M, Ziacchi M, Mitacchione G, Lavalle C, Saguner A, Lanfranchi A, Casalini G (2020) Arrhythmic safety of hydroxychloroquine in COVID-19 patients from different clinical settings. EP Europace 22(12):1855–1863
15. Chorin E, Wadhwani L, Magnani S, Dai M, Shulman E, Nadeau-Routhier C, Knotts R, Bar-Cohen R, Kogan E, Barbhaiya C (2020) QT interval prolongation and torsade de pointes in patients with COVID-19 treated with hydroxychloroquine/azithromycin. Heart rhythm 17(9):1425–1433
16. Tien JM (2017) Internet of things, real-time decision making, and artificial intelligence. Ann Data Sci 4(2):149–178
17. Shi Y (2022) Advances in big data analytics: theory, algorithms, and practices. Singapore, Springer Nature
18. Tessema T (2018) Modelling Under-Five Mortality among Hospitalized Pneumonia Patients in Hawassa City, Ethiopia: A Cross-Classified Multilevel Analysis. Ann Data Sci 5(2):111–132
19. Albahri AS, Hamid RA, Al-qays Z, Zaidan A, Zaidan B, Albahri AO, AlAmoodi A, Khlaf JM, Almahdi E, Thabet E (20202) Role of biological data mining and machine learning techniques in detecting and diagnosing the novel coronavirus (COVID-19): a systematic review. J Med Syst 44(7):1–11
20. Rautaharju PM, Surawicz B, Gettes LS (2009) AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part IV: the ST segment, T and U waves, and the QT interval a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol 53(11):982–991
21. Garg A, Lehmann MH (2013) Prolonged QT interval diagnosis suppression by a widely used computerized ECG analysis system. Circ Arrhythm Electrophysiol 6(1):76–83
22. Olson DL, Shi Y, Shi Y (2007) Introduction to business data mining. McGraw-Hill/Irwin, New York, pp 2250–2254
23. Kang SJ, Jung SI (2020) Age-Related Morbidity and Mortality among Patients with COVID-19. Infect Chemother 52(2):154–164
24. Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Fácila L, Ariza A, Nunez J, Cordero A (2020) The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. J Am Med Dir Assoc 21(7):915–918
25. Raimondi F, Novelli L, Ghirardi A, Russo FM, Pellegrini D, Biza R, Trapasso R, Giuliani L, Anelli M, Amoroso M (2021) Covid-19 and gender: lower rate but same mortality of severe disease in women—an observational study. BMC Pulm Med 21(1):1–11
26. Kazik A, Wilczek K, Poloński L (2010) Management of diastolic heart failure. Cardiol J 17(6):558–565
27. Wen W, Zhang H, Zhou M, Cheng Y, Ye L, Chen J, Wang M, Feng Z (2020) Arrhythmia in patients with severe coronavirus disease (COVID-19): a meta-analysis.Eur Rev Med Pharmacol Sci11395–11401
28. Antwi-Amoabeng D, Beutler BD, Singh S, Taha M, Ghuman J, Hanfy A, Manasewitsch NT, Ulanja MB, Ghuman J, Awad M (2021) Association between electrocardiographic features and mortality in COVID-19 patients. Ann Noninvasive Electrocardiol e12833
29. Barman HA, Atici A, Alici G, Sit O, Tugrul S, Gungor B, Okuyan E, Sahin I (2021) The effect of the severity COVID-19 infection on electrocardiography. m J Emerg Med 46:317–322
30. Zuin M, Rigatelli G, Roncon L, Zuliani G (2021) Left Bundle Branch Block and Mortality in COVID-19 Patients. Am J Cardiol 153:149–150
31. Ashtiyani M, Lavasani SN, Alvar AA, Deevband M (2018) Heart rate variability classification using support vector machine and genetic algorithm. J Biomed Phys Eng 8(4):423
32. Anderson HN, Bos JM, Haugaa KH, Morlan BW, Tarrell RF, Caraballo PJ, Ackerman MJ (2018) Prevalence and outcome of high-risk QT prolongation recorded in the emergency department from an institution-wide QT alert system. The Journal of emergency medicine 2018, 54(1):8–15

33. Niemeijer MN, van den Berg ME, Eijgelsheim M, Rijnbeek PR, Stricker BH (2015) Pharmacogenetics of drug-induced QT interval prolongation: an update. Drug Saf 38(10):855–867
34. Funck-Brentano C, Ouologuem N, Duparc S, Felices M, Sirima SB, Sagara I, Soulama I, Ouédraogo J-B, Beavogui AH, Borghini-Fuhrer I (2019) Evaluation of the effects on the QT-interval of 4 artemisinin-based combination therapies with a correction-free and heart rate-free method. Sci Rep 9(1):1–8
35. Cheung CC, Davies B, Gibbs K, Laksman ZW, Krahn AD (2020) Multilead QT screening is necessary for QT measurement: implications for Management of Patients in the COVID-19 era. Clin Electrophysiol 6(7):878–880
36. Mistry D, Hossain A, Sun J, Veenith T, Lall R, Bion J, Whitehouse T (2021) Beta-Blocker Treatment in Ventilated COVID-19 patients–A Cox Regression with Time Dependent Covariate Analysis. preprint, September 30th, Research Square. https://doi.org/10.21203/rs.3.rs-921813/v1
37. Regan W, O'Byrne L, Stewart K, Miller O, Pushparajah K, Theocharis P, Wong J, Rosenthal E (2021) Electrocardiographic changes in children with multisystem inflammation associated with COVID-19: associated with coronavirus disease 2019. J Pediatr 234:27–32e22
38. Sidek KA, Mai V, Khalil I (2014) Data mining in mobile ECG based biometric identification. J Netw Comput Appl 44:83–91
39. Utomo TP, Nuryani N, Nugroho AS (2021) A New Automatic QT-Interval Measurement Method for Wireless ECG Monitoring System Using Smartphone. J Biomed Phys Eng 11(5):641
40. Geleris J, Sun Y, Platt J, Zucker J, Baldwin M, Hripcsak G, Labella A, Manson DK, Kubin C, Barr RG (2020) Observational study of hydroxychloroquine in hospitalized patients with Covid-19. N Engl J Med 382(25):2411–2418
41. Cavalcanti AB, Zampieri FG, Rosa RG, Azevedo LC, Veiga VC, Avezum A, Damiani LP, Marcadenti A, Kawano-Dourado L, Lisboa T (2020) Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19. N Engl J Med 383(21):2041–2052
42. Group RC (2020) Effect of hydroxychloroquine in hospitalized patients with Covid-19. N Engl J Med 383(21):2030–2040

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