Original Article

Evaluation of Electrocardiographic Changes in Patients Under COVID-19 Treatment Regimes

Emre Özdemir, Uğur Karagöz, Selin Özdemir[1], Mustafa Ozan Gürsoy, Sadık Volkan Emren, Banu Karaca[2], Nihan Kahya Eren, Mustafa Karaca

Departments of Cardiology and [2]Infectious Diseases, Faculty of Medicine, Atatürk Research and Training Hospital, Katip Çelebi University, [1]Department of Infectious Diseases, Bozyaka Training and Research Hospital, Izmir, Turkey

ORCID:

Emre Özdemır: 0000-0003-0034-3022
Ugur Karagöz: 0000-0002-3983-0410
Selin Özdemır: 0000-0003-2298-4330
Mustafa Ozan Gürsoy: 0000-0001-8588-392X
Sadik Volkan Emren: 0000-0002-7652-1123
Banu Karaca: 0000-0003-1470-356X
Nihan Kahya Eren: 0000-0002-0232-7694
Mustafa Karaca: 0000-0002-5060-1045

Abstract

Background and Aim: Awareness of electrocardiographic (ECG) changes is crucial in patients who receive coronavirus disease 2019 (COVID-19) treatment. In this study, we aimed to evaluate ECG parameters in patients under COVID-19 therapy and their relationship with the severity of lung involvement and the disease on the basis of thoracic computerized tomography (TCT) findings and laboratory parameters. **Materials and Methods:** Of 350 patients hospitalized due to COVID-19 between March 2020 and June 2020, 300 patients with available data were retrospectively analyzed. Blood analysis, electrocardiographic, and clinical findings were evaluated. Six-month follow-up data were also recorded. **Results:** The patients were categorized into two groups: survivor (n = 206, 68.7%, Group 1) and nonsurvivor patients (n = 94, 31.3%, Group 2). The mean total follow-up period was 125.39 ± 73.09 days. The mean age was similar in both groups. In multivariate regression analysis that aimed to predict COVID-19 disease severity, it was found that besides increased C-reactive protein and D-dimer levels, and ≥50% lung involvement in TCT, which are well known as bad prognostic factors, the corrected QT interval duration (QTc) prolongation ≥60 miliseconds (msn) during hospitalization was associated with worse prognosis in COVID-19 patients during follow-up. **Conclusion:** Our study is the first study that demonstrated that the presence of ≥60 msn QTc prolongation during hospital stay was found to be the most valuable ECG parameter to predict the prognosis and had a significant association with ≥50% lung involvement in TCT in patients under anti-COVID therapy. Close monitoring of this ECG parameter is important both in terms of treatment planning and interpretation of disease progression.

Keywords: COVID-19, electrocardiographic, mortality, myocardial injury, severity

Introduction

The world encountered a new virus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in 2019.[1] The surface spike protein of SARS-CoV-2 binds to the human angiotensin-converting enzyme-2 (ACE2) receptor.[2] ACE2 is expressed in the lungs, heart, intestinal epithelium, vascular endothelium, and kidneys, thereby providing a mechanism for the multiorgan dysfunction that can be seen with SARS-CoV-2 infection.[3] The clinical manifestation of SARS-CoV-2 is associated with ACE2R presence, so it is predominantly associated with respiratory system disease

Received: 22-07-2022 **Revised:** 01-10-2022 **Accepted:** 05-10-2022
Published Online: 29-11-2022

Access this article online

Quick Response Code:

Website: http://www.ijcva.com

DOI: 10.4103/ijca.ijca_14_22

Address for correspondence: Dr. Emre Özdemir, Departments of Cardiology, Faculty of Medicine, Atatürk Research and Training Hospital, Katip Çelebi University, Karabaglar, Izmir, Turkey.
E-mail: emreozdemir27@yahoo.com.tr

How to cite this article: Özdemir E, Karagöz U, Özdemir S, Gürsoy MO, Emren SV, Karaca B, *et al*. Evaluation of electrocardiographic changes in patients under COVID-19 treatment regimes. Int J Cardiovasc Acad 2022;8:96-101.

but can also affect the cardiovascular system as a result of multisystemic involvement. This new viral disease has been named as coronavirus disease-2019 (COVID-19).[4]

Several studies have reported that elevated levels of cardiac markers such as cardiac troponin and electrocardiographic (ECG) or echocardiographic abnormalities can accompany other inflammatory markers depending on the disease severity.[3,5] These effects may be an extension of systemic disease and hypoxia or could be associated with acute coronary syndrome and decompensated heart failure (HF).[6] Cardiovascular effects have been reported to be present in 7.2% of all patients and 22% of the patients followed up in intensive care units.[7] It has also been suggested that the medication used for COVID-19 treatment, including chloroquine, hydroxychloroquine, azithromycin, and lopinavir/ritonavir can cause ECG changes, especially QT or PR prolongation.[8]

ECG is the first step test for the diagnosis of cardiac disorders. In patients with COVID-19 disease, the importance of ECG changes is still undefined.[9,10] This study aimed to evaluate ECG parameters in patients under COVID-19 therapy and their relationship with the severity of lung involvement and the disease on the basis of thoracic computerized tomography (TCT) findings and laboratory parameters.

Materials and Methods

Patient selection

A total of 350 patients who were hospitalized due to COVID-19 disease between March 2020 and June 2020 in our hospital were collected. All of the patients presented at the emergency department with respiratory symptoms, and TCT revealed findings compatible with COVID-19. Due to the absence of basal and follow-up medical records, 50 patients were excluded from the study. The remaining 300 patients who had been followed up for 6 months were retrospectively analyzed.

Data collection

After hospitalization, a standard clinical examination was performed. Blood tests were obtained for the evaluation of complete blood count-hemogram (CBC-Hg), creatinine, blood urea nitrogen, troponin I (TI), and C-reactive protein (CRP) levels. Furthermore, 12-lead ECG, heart rate (HR), PR- QRS-corrected QT interval duration (QTc) and the change in PR-QRS - QTc duration ([duration at control ECG]- [duration on admission ECG]) were calculated as milliseconds (msn). The presence of any ST segment change, left or right bundle block, was noted.

The QT duration was measured as the interval between the start of the Q wave and the end of the T wave, and corrected by HR as per the Bazett formula. The PR duration was measured as the interval between the start of the *P* wave and the end of the R wave. The QRS duration was measured as the interval from the start of the Q wave to the end of the S wave.

The presence of comorbidities (arterial hypertension [AHT], coronary arterial disease [CAD], chronic obstructive pulmonary disease [COPD], diabetes mellitus [DM], HF, and chronic renal disease [CRD]) was recorded on the basis of documented medical history. AHT was defined as arterial pressure regulated with medication or diet, DM as blood glucose regulated with medication or diet, and CAD was defined when a history of >50% coronary lesion or acute coronary syndrome is present. HF was defined as left ventricular ejection fraction (LVEF) <50% on echocardiography. COPD was defined on the basis of a diagnosis made by a pulmonologist. CRD was defined as low glomerular filtration rate (GFR) for age.

The usage of hydroxychloroquine (HCQ) and macrolide was also noted, as they are known to cause QT prolongation associated with COVID-19 treatment.

The patients were evaluated by two-dimensional transthoracic echocardiography in case of any cardiac symptoms or elevated TI or significant ECG changes. All of these data were retrieved retrospectively from the hospital medical records.

The involvement of lung infiltration was defined on the basis of TCT findings (as ≥50% or <50%). The incidence of in-hospital mortality, mortality during the follow-up period after discharge, and follow-up duration (period from admission to mortality or last outpatient clinic visit) were recorded retrospectively.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software version 21 (IBM, NY, USA). Data were presented as mean ± standard deviation values for continuous variables and as number (*n*) and percentage (%) for categorical variables. Differences in proportions between groups were analyzed using the Chi-square test. The mean values of variables were compared using the Mann–Whitney *U*-test based on the distribution of continuous variables. Univariate and multivariate Cox regression analyses were used to define independent risk factors for mortality. Factors in univariate analyses with a $P < 0.1$ were included in the multivariate survival analyses according to certain risk factors and were evaluated using Kaplan–Meier analyses. In two-tailed tests, $P < 0.05$ were considered statistically significant.

Ethical statement

All procedures were performed with the informed consent of the patients. Approval for the study was granted by the Local Ethics Committee (Approval date 02.07.2020, number 786).

Results

The study population ($n = 300$) was divided into two groups as survivor (Group 1; $n = 206$, 68.7%) and (Group 2; $n = 94$, 31.3%) groups. The mean total follow-up period for both groups was 125.39 ± 73.09 days and 31.33 ± 33.05 days for the nonsurvivor group. The results of this study showed that 206 (68.7%) patients were discharged uneventfully (survivor group). In our study, the median (interquartile range [IQ]) age of the patients was 62 (48–72) years in the survivors and 70 (61–80) years in the nonsurvivors ($P < 0.001$) [Table 1].

The presence of AHT, DM, CAD, HF, and gender distribution did not show any statistically significant difference between the two groups. The presence of CRD (patients with GFR <30), COPD, pulmonary infiltration, and the median age was statistically significant between the two groups [Table 1]. There was also no statistically significant difference regarding the use of hydroxychloroquine (Group 1: n = 192 (93%); Group 2: n = 87 (93%), P = 0.603) and macrolide (azithromycin) (Group 1: n = 130 (63%); Group 2: n = 60 (64%), P = 0.815) as QT-prolonging medications used in COVID-19 treatment [Table 1].

A statistically significant difference was detected between the two groups regarding mean LVEF, white blood cell (WBC), lymphocyte (LYM) count, hemoglobin (Hb), and platelet (PLT) counts, peak D-dimer values and peak TI [Table 2].

Table 1: Comparison of demographic and clinical features of the two groups

Variable	Survivors (Group 1), *n* (%)	Nonsurvivors (Group 2), *n* (%)	*P*
Female gender	82 (39.8)	42 (45)	0.426
Age (years), median (IQR)	62 (48-72)	70 (61-80)	<0.001
AHT	102 (49)	54 (57)	0.202
DM	54 (26)	32 (34)	0.164
CAD	54 (26)	31 (33)	0.228
HF	26 (13)	16 (17)	0.308
COPD	33 (16)	24 (25)	0.051
CRD (GFR <30 ml/min/1.73 m^2)	29 (14)	30 (32)	0.001
Presence of pulmonary infiltration	4 (2)	27 (29)	<0.001
Macrolide usage (azithromycin)	130 (63)	60 (64)	0.815
Hydroxychloroquine usage	192 (93)	87 (93)	0.603

GFR: Glomerular filtration rate, COPD: Chronic obstructive pulmonary disease, CRD: Chronic renal disease, AHT: Arterial hypertension, DM: Diabetes mellitus, CAD: Coronary arterial disease, HF: Heart failure, IQR: Interquartile range

Table 2: Comparison of laboratory features in the two groups

Variable	Median (IQR)		*P*
	Survivors (Group 1)	Non-survivors (Group 2)	
LVEF (%)	50 (35-60)	60 (40-60)	0.095
WBC (/L)	7495 (5412-9745)	11,980 (7795-16,860)	<0.001
NEU (/L)	4750 (3272-6680)	10,060 (6700-14,932)	<0.001
LYM (/L)	1495 (1060-2115)	910 (527-1335)	<0.001
Hb (g/dL)	12.5 (10.9-14.3)	10.8 (8.9-12)	<0.001
PLT (×10^3/L)	227 (18-293.5)	241.5 (171-355)	0.440
CRP (mg/dL)	23 (6.7-69)	101 (38.5-178)	<0.001
PDD (mcg/L)	349 (177-937)	2558 (985-6253)	<0.001
Peak TI (ng/L)	0 (0-0)	0.34 (0-1.27)	<0.001

LVEF: Left ventricular ejection fraction, WBC: White blood cell, NEU: Neutrophil, LYM: Lymphocyte, Hb: Hemoglobin, PLT: Platelet, CRP: C-reactive protein, TI: Troponin I, PPD: Peak D-dimer, SD: Standard deviation, IQR: Interquartile range

The comparison of mean basal HR, PR, and QRS duration at hospital admission, control HR, control PR, control QTc duration, change in QTc duration, presence of ≥60 msn QTc prolongation, the presence of ST segment change during hospitalization also showed a significant difference between the groups [Table 3]. However, in our population, no arrhythmia associated with QT prolongation was detected in any patients.

The univariate analysis was performed to estimate prognosis due to COVID-19 pneumonia. The GFR <30, age >65 years, WBC (10–20, 20–30, ≥30 × 10^3/L), neutrophil (NEU) (≤1, >5 x10^3/L), LYM (≤1 × 10^3/L); CRP (≥50 mg/dL), D-dimer (≥1000 mcg/L), TI (≥0.1 ng/mL); extension of lung infiltration ≥50% in TCT, basal HR ≥100/min during admission, control HR ≥100/min; control QTc ≥500 ms; the presence of ≥60 ms QTc prolongation and presence of ST change during hospitalization found to be different between the groups. But on multivariate regression analysis, only NEU >5 × 10^3/L, LYM ≤1 × 10^3/L, CRP ≥50 mg/dL, D-dimer ≥1000 mcg/L, extension of lung infiltration ≥50% in TCT, and presence of QTc prolongation ≥60 ms during hospitalization were found to be associated with worse prognosis [Table 4].

Discussion

In this study, QTc prolongation ≥60 msn during hospitalization was found to be the most valuable ECG parameter in COVID-19 patients. This prolongation was not found to be associated with the usage of HCQ (P = 0.603) between the two groups.

Cardiac involvement in COVID-19 can be categorized into five types: (1) cardiac injury (mainly due to ischemia or myocarditis), (2) cardiac arrhythmia, (3) new-onset or worsening of heart failure, (4) thromboembolic disease, and (5) cardiac abnormalities induced by COVID-19 treatment.[11] As a cost-effective tool, ECG is one of the best methods that determine cardiac involvement and the effects of medications in patients who suffer from COVID-19. Furthermore, it offers the possibility of remote evaluation.[12] Current data regarding the evaluation of ECG changes during hospitalization in patients with COVID-19 are limited. In this study, ECG evaluation was made in 300 patients who were hospitalized due to COVID-19 pneumonia.

There are mainly four proposed mechanisms regarding cardiac involvement and ECG changes: (1) ACE2 is highly expressed in heart tissue, and therefore, SARS-CoV2 can cause direct cardiac damage, (2) Systemic hypoxemia due to COVID-19 may lead to myocardial injury, (3) Systemic inflammatory response may cause myocardial involvement, and (4) ECG changes may be associated with the side-effects of COVID-19 treatment (such as QT prolongation due to chloroquine and azithromycin).[13] Cardiac involvement in patients with COVID-19 is reflected on ECG as QRS or ST segment changes, QT or PR prolongation, and atrial or ventricular arrhythmias. Furthermore, nonspecific ECG findings have been reported in

Table 3: Comparison of electrocardiogram parameters and changes in the two groups

Variable	Median (IQR)		*P*
	Survivors (Group 1)	Nonsurvivors (Group 2)	
Basal HR during admission (/mn)	85 (74-98)	96 (84-115)	<0.001
Basal QRS during admission (msn)	88 (80-98)	82 (76-98)	0.010
Basal QTc during admission (msn)	428 (409-450)	436 (415-455)	0.298
Control QRS during hospitalization (msn)	92 (82-100)	90 (78-110)	0.547
QTc during hospitalization (msn)	435 (415-457)	479 (452-499)	<0.001
QTc ≥500 msn during hospitalization, *n* (%)	10 (5)	23 (25)	<0.001
QRS duration change during hospitalization (msn)	2 (−2-6)	3 (−2-16)	0.051
QTc duration change during hospitalization (msn)	5 (−7-20)	40 (24-64)	<0.001
QTc longation ≥60 msn during hospitalization, *n* (%)	4 (2)	30 (32)	<0.001
Presence of ST segment change during hospitalization, *n* (%)	68 (33)	63 (67)	<0001

ECG: Electrocardiogram, HR: Heart rate, PR: PR interval duration, QRS: QRS interval duration, QTc: Corrected QT interval duration, IQR: Interquartile range

Table 4: Comparison of independent predictors to estimate the mortality due to coronavirus disease 2019 pneumonia

Variable	Univariate analysis				Multivariate logistic regression analysis*			
	HR	95% CI		*P*	HR	95% CI		*P*
COPD	1.562	0.982	2.485	0.06	1.758	0.726	4.256	0.211
GFR <30 ml/min/1.73 m^2	2.387	1.545	3.688	<0.001	1.593	0.678	3.744	0.285
Age >65 (years)	3.099	1.840	5.217	<0.001	1.859	0.824	4.193	0.135
LVEF <40%	1.949	0.643	5.908	0.24				
WBC (RR: <10×10^3/L)								
10-20×10^3/L	3.967	2.551	6.171	<0.001				
20-30×10^3/L	4.009	1.923	8.356	<0.001				
≥30×10^3/L	9.412	3.326	26.639	<0.001				
NEU (RR: 1-5×10^3/L)								
≤1×10^3/L	13.415	3.689	48.788	<0.001	1.562	0.160	15.256	0.701
>5×10^3/L	4.187	2.068	8.447	<0.001	3.105	1.247	7.731	0.015
LYM (RR: 1-3×10^3/L)								
≤1×10^3/L	3.494	2.304	5.297	<0.001	3.809	1.738	8.347	0.001
Hg change (for decrease of one unit) (g/dL)	1.002	0.999	1.004	0.25				
CRP 500 (mg/dL)	1.012	1.009	1.016	<0.001	1.009	1.004	1.015	0.002
D-dimer ≥1000 (mcg/L)	5.990	3.781	9.492	<0.001	3.384	1.557	7.352	0.002
TI≥0.1 (ng/mL)	6.317	4.126	9.671	<0.001				
Extension of lung infiltration on TCT ≥50%	8.917	5.573	14.268	<0.001	9.699	2.658	35.383	0.001
Basal HR >100 (/min)	2.727	1.609	4.622	<0.001	1.153	0.467	2.847	0.757
Basal QRS ≥120 (msn)	0.827	0.383	1.787	0.63				
Control QTc ≥500 msn during hospitalization	3.467	2.161	5.565	<0.001				
Presence of ≥60 msn QTc prolongation	6.192	3.977	9.639	<0.001	12.360	4.238	36.042	<0.001
Presence of ST change	3.193	2.075	4.915	<0.001	0.984	0.439	2.204	0.969

*Therefore, due to the significant correlation between WBC and neutrophil values. Presence of QTc ≥60 msn prolongation during hospitalization and basal QTc ≥500 msn at admission. D-dimer and TI values, the variables of QTc ≥500 msn during hospitalization, TI and WBC levels were not put in the multivariate logistic regression model. HR: Heart rate, QRS: QRS interval duration, QTc: Corrected QT interval duration, GFR: Glomerular filtration rate, COPD: Chronic obstructive pulmonary disease, LVEF: Left ventricular ejection fraction, WBC: White blood cell, NEU: Neutrophil, LYM: Lymphocyte, CRP: C-reactive protein, TI: Troponin I, TCT: Thoracic computed tomography, CI: Confidence interval, HR: Hazard ratio, RR: Reference range, Hg: Hemogram

COVID-19 associated with hypoxia or inflammatory damage. In addition, tachycardia, which is defined as >90–100/bpm HR, has been associated with mortality and worsening of COVID-19.[14] Consequently, ECG changes tend to be associated with worse prognosis in COVID-19 patients.

The mortality rate of the present study was similar to data reported by Huang *et al*.[15] Consistent with previous studies, mortality was higher in older patients. This is probably because the hospitalized population was predominantly composed of old patients with worse clinical conditions.[4]

Various studies have shown that DM, AHT, CAD, obesity, CKD, and COPD are the most common comorbid diseases observed in COVID-19 patients and are known to be associated with worse COVID-19 outcomes.[16-19] Consistent with previous studies, the most common comorbid diseases in the current study were AHT, DM, CAD, HF, and COPD, in decreasing

order [Table 1]. A statistically significant association was only determined between CRD and mortality ($P < 0.001$) [Table 1].

The major abnormal laboratory findings in cases with COVID-19 include elevated CRP, lymphopenia, leukopenia, and thrombocytopenia.[20] Reade *et al*.[21] reported that COVID-19 patients with low hemoglobin are associated with high mortality rates. Hence, several laboratory parameters, such as leukocytosis, elevated cardiac troponins as a marker of cardiac injury, thrombocytopenia, neutrophilia, lymphopenia, and high CRP levels, predict clinical worsening and poor survival in patients with COVID-19.[14,22,23] Consistent with these data, the WBC, NEU, CRP, peak D-dimer, and peak TI levels were found to be significantly higher, and LYM, Hb, and PLT levels were found to be significantly lower in Group 2 compared to Group 1 in the current study[Table 2]. In the univariate analysis, TI level was found to have a statistically significant association with mortality, whereas LVEF values were similar between the two groups. This may indicate that early myocardial injury shown by significant TI increase could not be detected by LVEF [Table 4].

Li *et al*.[24] showed a relationship between lesion extension in TCT scans and clinical deterioration of COVID-19. Consistent with this finding, the current study showed that ≥50% lung infiltration in TCT scans was significantly associated with increased mortality [Table 4]. This variable has been considered valuable for the determination of the severity of pulmonary involvement and disease progression.

There are limited data regarding ECG changes and increased mortality. Wang *et al*.[25] resented abnormal ECG in most of the COVID-19 patients and detected that ST-T change was the most important clinical evidence in the abnormal ECG. Pavri *et al*.[26] showed that 50.7% of their COVID-19 patients had PR interval change and increased HR. Angeli *et al*.[9] declared that ST-T abnormality was present in 30% of the COVID-19 patients in their study. Santoro *et al*. reported QT prolongation in some of their COVID-19 population, and Jain *et al*.[27,28] stated that QT prolongation can be caused by COVID-19 medications.

In light of these data, we aimed to determine the ECG parameters that could affect disease surveillance, such as the extension of lung involvement in TCT and laboratory parameters. In our study, tachycardia at admission, QRS duration change, ST segment changes, and QT duration prolongation showed a statistical significance on univariate analysis.

The current study showed that the presence of ≥60 msn QTc prolongation during hospitalization (HR = 12,360; 95% confidence interval [CI]: 4238–36,042; $P \leq 0.001$), extension of ≥%50 lung infiltration in TCT (HR = 9,699; 95% CI: 2658–35,383; $P = 0.001$), D-dimer ≥1000 mcg/L (HR = 3384, 95% CI: 1557–7352; $P = 0.002$), CRP ≥500 mg/dL (HR = 1009; 95% CI: 1004–1015; $P = 0{,}002$), LYM ≤1 $\times 10^3$/L (HR = 3809; 95% CI: 1738–8347; $P = 0001$), NEU >5 $\times 10^3$/L (HR = 3105; 95% CI: 1247–7731; $P = 0015$) were independent predictors for mortality in multivariate logistic regression analysis [Table 4 and Figure 1].

Study limitations

The main limitation of our study was that it was a retrospective and single-center study.

Conclusion

In conclusion, to the best of our knowledge, this is the first study that investigates the relationship between ECG changes

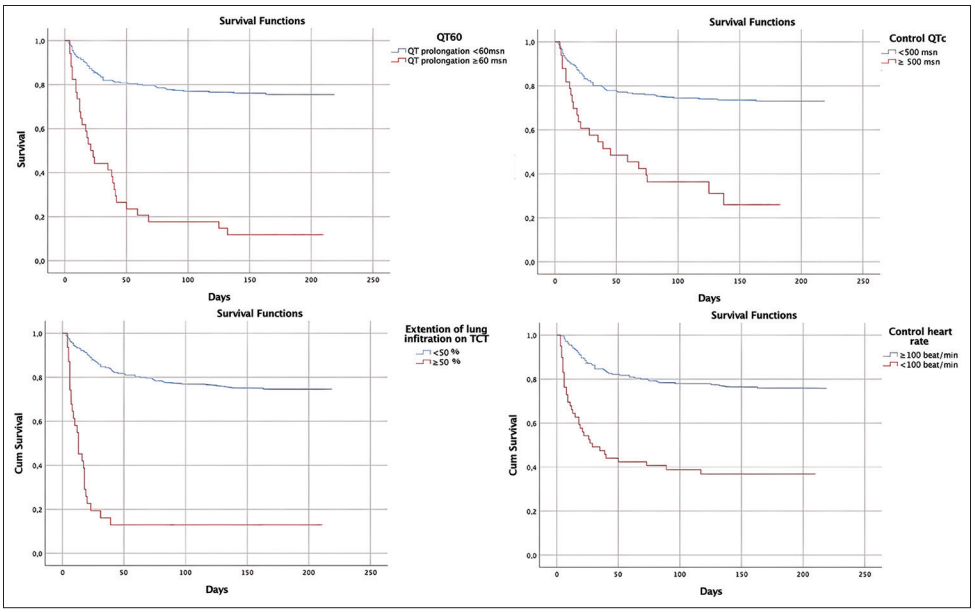

Figure 1: Control QTc, QTc prolongation, control heart rate, and thoracic computed tomography findings associated with mortality and survival. QTc: Corrected QT interval duration

and laboratory parameters and lung involvement severity in TCT in patients with COVID-19. We have shown that the presence of ≥60 msn QTc prolongation during hospitalization was the most valuable parameter to predict the prognosis and had a significant association with ≥50% lung involvement in TCT in patients under anti-COVID-19 therapy. Therefore, close monitoring of ECG, especially QTc prolongation ≥60 msn during the hospital stay, is important both in terms of treatment planning and interpretation of disease progression.

Declaration of patient consent

All procedures are performed after the patients' verbal or written consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease; 2019 (COVID-19). Available from: https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(COVİD-19). Published; 2020. [Last accessed on 2020 Nov 11].
2. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, *et al.* SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and Is blocked by a clinically proven protease ınhibitor. Cell 2020;181:271-80.e8.
3. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, *et al*. COVID-19 and cardiovascular disease. Circulation 2020;141:1648-55.
4. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, *et al.* Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. J Infect 2020;80:388-93.
5. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, *et al*. Cardiovascular ımplications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:811-8.
6. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, *et al*. The variety of cardiovascular presentations of COVID-19. Circulation 2020;141:1930-6.
7. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-ınfected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
8. Sacher F, Fauchier L, Boveda S, de Chillou C, Defaye P, Deharo JC, *et al*. Use of drugs with potential cardiac effect in the setting of SARS-CoV-2 infection. Arch Cardiovasc Dis 2020;113:293-6.
9. Angeli F, Spanevello A, De Ponti R, Visca D, Marazzato J, Palmiotto G, *et al*. Electrocardiographic features of patients with COVID-19 pneumonia. Eur J Intern Med 2020;78:101-6.
10. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, *et al.* Association of cardiac ınjury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:802-10.
11. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: A review. JAMA Cardiol 2020;5:831-40.
12. Haseeb S, Gul EE, Çinier G, Bazoukis G, Alvarez-Garcia J, Garcia-Zamora S, *et al*. Value of electrocardiography in coronavirus disease 2019 (COVID-19). J Electrocardiol 2020;62:39-45.
13. He J, Wu B, Chen Y, Tang J, Liu Q, Zhou S, *et al*. Characteristic electrocardiographic manifestations in patients With COVID-19. Can J Cardiol 2020;36:966.e1- 966.e4.
14. Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, *et al*. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. PLoS One 2020;15:e0241955.
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.
16. Tang D, Comish P, Kang R. The hallmarks of COVID-19 disease. PLoS Pathog 2020;16:e1008536.
17. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA 2020;323:2052-9.
18. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 – United States, february 12-march 28, 2020. MMWR Morb Mortal Wkly Rep 2020;69:382-6.
19. Alyammahi SK, Abdin SM, Alhamad DW, Elgendy SM, Altell AT, Omar HA. The dynamic association between COVID-19 and chronic disorders: An updated insight into prevalence, mechanisms and therapeutic modalities. Infect Genet Evol 2021;87:104647.
20. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, *et al*. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis 2020;34:101623.
21. Reade MC, Weissfeld L, Angus DC, Kellum JA, Milbrandt EB. The prevalence of anemia and its association with 90-day mortality in hospitalized community-acquired pneumonia. BMC Pulm Med 2010;10:15.
22. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, *et al*. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43.
23. Fan BE, Chong VC, Chan SS, Lim GH, Lim KG, Tan GB, *et al*. Hematologic parameters in patients with COVID-19 infection. Am J Hematol 2020;95:E131-4.
24. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, *et al.* Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 2020;146:110-8.
25. Wang Y, Chen L, Wang J, He X, Huang F, Chen J, *et al*. Electrocardiogram analysis of patients with different types of COVID-19. Ann Noninvasive Electrocardiol 2020;25:e12806.
26. Pavri BB, Kloo J, Farzad D, Riley JM. Behavior of the PR interval with increasing heart rate in patients with COVID-19. Heart Rhythm 2020;17:1434-8.
27. Santoro F, Monitillo F, Raimondo P, Lopizzo A, Brindicci G, Gilio M, *et al*. QTc Interval prolongation and life-threatening arrhythmias during hospitalization in patients with coronavirus disease 2019 (COVID-19): Results from a multicenter prospective registry. Clin Infect Dis 2021;73:e4031-8.
28. Jain S, Workman V, Ganeshan R, Obasare ER, Burr A, DeBiasi RM, *et al*. Enhanced electrocardiographic monitoring of patients with coronavirus disease 2019. Heart Rhythm 2020;17:1417-22.