The role of ECG as a mortality predictor in COVID-19 patients treated in the intensive care unit

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ABSTRACT

Background: COVID-19 infection has reached serious morbidity and mortality rates all over the world for a short time. Many studies have investigated the relationship of COVID-19 disease with mortality and morbidity. In this study, we wanted to elucidate the relationship between rhythm character (sinus rhythm vs atrial fibrillation) and QTc and frontal plane QRS-T angle, which parameters are reflecting the depolarization-repolarization kinetics, and mortality, which were not emphasized enough in previous studies.

Material and Method: 259 patients admitted to the intensive care unit due to COVID-19 infection between 01.04.2020 and 01.12.2020 was included in the study. The demographic characteristics of the patients, clinical backgrounds, laboratory values at the time of admission to the intensive care unit, and 12 derivation ECG records were obtained from the patient files. Rhythm, PR distance, QRS duration and morphology, QT interval, T wave morphology, presence of atrioventricular (AV) block, QRS axis, presence of ventricular premature contraction, frontal plane QRS-T (f(QRS-T)) angle degree were determined on 12 derivation ECG records. Patient groups were classified as "deceased patient" and "survivors" and the relationship of these parameters with survival was tried to be elucidated.

Results: the frequency of atrial fibrillation was significantly higher in the "deceased patient" group. For patients in sinus rhythm, there was no difference between the two groups in terms of PR distance and 1st degree AV block. Severe AV block was not observed in either group. There was no difference between the two groups in terms of QRS morphology, T wave inversion, and ventricular premature contractions. QRS duration, corrected QTc duration, and frotal plane QRS-T angle values were found to be statistically significantly higher in in the "deceased patient" group.

Conclusion: Atrial fibrillation, prolonged QTc duration and increased frontal plane QRS-T angle can be considered as mortality predictors in COVID-19 infection whose mortality rate is high all over the world.

Keywords: COVID-19, ECG, AF, QRS-T angle, mortality

INTRODUCTION

COVID-19 disease, caused by the severe acute respiratory syndrome Coronavirus 2 (SARS-Cov-2) virus, continues to affect the whole world for more than a year. The rate of spread of the infection is very high, as the number of infected patients increases, morbidity and mortality numbers also increase (1,2). Pneumonia caused by the COVID-19 disease creates respiratory stress, and the need for non-invasive or invasive mechanical ventilation support may arise. With the treatment administered in the intensive care unit, clinical recovery occurs as well as mortality.

Electrocardiography (ECG) is one of the most frequently used diagnostic tests in clinical practice. Many studies have shown the prognostic significance of ECG findings in many diseases, especially in cardiovascular system diseases. Information on COVID-19 infection is newly accumulating, and information on the clinical course and mortality of COVID-19 is emerging with the studies. In the early stages of Covid 19 infection, ECG findings - especially QTc value - were used to determine treatment options and side effects of treatment (3). In addition, studies related to Covid 19 mortality and ECG findings are also published. In addition, studies related to Covid 19 mortality and ECG findings have begun to be published. Our aim in this study is to reveal the relationship between in-hospital mortality and data and parameters to be obtained from 12-lead ECGs of patients who have been followed up in intensive care with COVID-19 infection.

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MATERIAL AND METHOD

259 patients admitted to the intensive care unit due to COVID-19 infection between 01.04.2020 and 01.12.2020 were included in the study. The demographic characteristics of the patients, clinical backgrounds, laboratory values at the time of admission to the intensive care unit, and 12 derivation ECG records were obtained from the patient files. Rhythm, PR distance, QRS duration and morphology, QT interval, T wave morphology, presence of atriventricular (AV) block, QRS axis, presence of ventricular premature contraction, frontal plane QRS-T (f(QRS-T)) angle degree were determined on 12 derivation ECG records. Patient groups were classified as "deceased patient" and "survivors" and the relationship of these parameters with survival was tried to be elucidated. This retrospective study was carried out with the permission of Keçiören Trainig and Research Hospital Clinical Researchs Ethics Committee (Date: 22.12.2020, Decision No: 15/2206). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

12 leads ECG recordings were performed at a speed of 25mm/sec and with a height of 10 mm/mV. In 12 derivations ECG, recordings with irregular R-R distance without P waves were accepted as atrial fibrillation (AF). Recordings longer than 120 milliseconds were defined as Right Bundle Branch Block or Left Bundle Branch Block according to their morphology. Other wide QRS morphology that does not fit this classification was collected under the interventricular conduction defect (IVCD). The corrected QT (QTc) distance is calculated according to the Bazett formula. All ECG records had automatically reported QRS axis and T axis data. The angle f(QRS-T) was calculated from these angles as the distance between the QRS axis and the T axis.

Statistical Analysis

SPSS for Windows version 23.0 (SPSS Inc., IL, USA) was used for statistical analysis. Continuous variables were expressed as means± standard deviations and categorical variables were expressed as percentages. Continuous data were compared using Student's t test. Categorical data were compared using the chi-square test. With ch square test, Pearson's correlation coefficient was used for correlation analysis. A value of $p < 0.05$ was considered statistically significant.

RESULTS

When the patient groups were compared, the mean age was higher in the "deceased patient" group (71.15±10.75 vs. 63.09±12.69; p<0.001). When co-morbidities were taken into account, heart failure and history of cerebrovascular events were statistically significantly higher in the "deceased patient" group, while there was no statistically significant difference in terms of hypertension, coronary artery disease, diabetes mellitus, malignancy, chronic obstructive pulmonary disease and gender (**Table 1**).

When ECG parameters were examined, the frequency of atrial fibrillation was significantly higher in the "deceased patient" group. For patients in sinus rhythm, there was no difference between the two groups in terms of PR distance and 1st degree AV block. Severe AV block was not observed in either group. There was no difference between the two groups in terms of QRS morphology, T wave inversion, and ventricular premature contractions. QRS duration, corrected QTc duration, and frotal plane QRS-T angle values were found to be statistically significantly higher in in the "deceased patient" group (**Table 2**).

Tablo 1. Demographic, clinical and laboratory characteristics of the study patients			
	Died n=101	Survived n=158	P value
Age	71.15±10.75	63.09±12.69	<0.001
Gender			0.171
Female	33 (32.7%)	65 (41.1%)	
Male	68 (67.3%)	93 (58.9%)	
Hypertension	44 (43.6%)	81 (51.3%)	0.226
Diabetes mellitus	23 (22.8%)	38 (24.1%)	0.813
Coronary artery disease	21 (20.8%)	28 (17.7%)	0.538
Heart failure	9 (8.9%)	5 (3.2%)	0.046
Chronic obstructive pulmonary disease	16 (15.8%)	21 (13.3%)	0.567
Malignancy	6 (5.9%)	12 (7.6%)	0.610
Cerebrovascular event	8 (7.9%)	4 (2.5%)	0.044
Glucose (mg/dL)	189.55±96.22	175.69±99.48	0.270
Creatinine (mg/dL)	1.22±0.44	1.01±0.31	<0.001
GFR (mL/min)	61.51±23.11	80.53±78.19	0.018
Albumine (mg/dL)	3.05±0.46	3.36±0.61	<0.001
AST (IU/L)	69.89±93.02	43.57±39.29	0.002
ALT (IU/L)	51.61±77.61	37.54±42.01	0.061
GGT (IU/L)	69.44±83.69	64.10±83.19	0.616
LDH (IU/L)	639.64±428.56	391.51±185.71	<0.001
CRP (mg/dL)	141.93±99.01	109.52±99.40	0.011
Ferritin (ng/mL)	791.42±522.57	465.60±459.42	<0.001
D-dimer (mg/L)	6.85±15.19	2.93±9.33	0.012
Troponin (ng/L)	532.45±2459.57	33.79±177.63	0.012
Lactate (mmol/L)	3.43±2.50	1.21±0.81	<0.001
Sat O_2 (%)	74.07±8.78	85.79±7.82	<0.001
WBC (×10³/µL)	12.4899±6.2614	8652.6±3866.1	<0.001
Neutrophile (×10³/µL)	10.8151±5.8133	7008.4±3917.7	<0.001
Lymphocyte (×10³/µL)	992.2±1671.9	1139.1±616.7	0.317
Platelet	241144±113290	257284±98665	0.227
Hgb (g/dL)	13.37±2.18	13.34±1.65	0.903

(ALT: alanine aminotransferase, AST: aspartate transaminase, CRP: C-reactive protein, GFR: Glomerular Filtration rate, GGT: gamma-glutamyl transpeptidase, Hgb: hemoglobin, LDH: lactic acid dehydrogenase, WBC: white blood cell)

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Table 2. ECG findings and characteristics of the study patients			
	Died n=101	Survived n=158	P value
Heart rate (b.p.m)	102.68±25.04	90.77±19.14	<0.001
Rythm			<0.001
Sinus Rythm	83 (82.2%)	157 (99.4%)	
Atrial Fibrillation	18 (17.8%)	1 (0.6%)	
PR interval (msec)	152.70±24.10	154.31±28.48	0.796
First degree AV block	3 (3.6%)	8 (5.1%)	0.602
QRS (msec)	95.77±16.53	92.04±13.83	0.051
QRS morphology			0.489
Normal	77 (76.2%)	129 (81.6%)	
IVCD	15 (14.9%)	22 (13.9%)	
LBBB	6 (5.9%)	4 (2.5%)	
RBBB	3 (3.0%)	3 (1.9%)	
Ventricular premature contraction	14 (13.9%)	16 (10.1%)	0.360
Corrected QT (msec)	426.75±35.50	416.97±25.66	0.011
T wave inversion	14 (13.9%)	11 (7.0%)	0.067
Abnormal QRS axis	50 (49.5%)	50 (31.6%)	0.004
Frontal Plane QRS-T angle (0)	64.96±52.69	37.90±34.43	<0.001
IVCD: interventricular conduction disease, LBBB: left bundle brunch block, RBBB: right bundle brunch block			

As an acute phase reactant, albumin levels were significantly lower in the "deceased patient" group, and ferritin and C-reactive protein (CRP) levels were significantly higher in the "deceased patient" group. There was a statistically significant difference between the two groups in terms of creatinine, glomerule filtration rate (GFR), aspartate transaminase (AST), lactic acid dehydrogenase (LDH), troponin, d-dimer, lactate and Sat O₂, white blood count (WBC), neutrophil count (**Table 1**).

DISCUSSION

COVID-19 infection rapidly affected the whole world, reaching high mortality rates with the increase in the number of infected patients and the respiratory stress it caused. The fact that the infection is caused by a newly emerging virus limits the diagnosis and treatment options, and as the knowledge about the disease increases, knowledge about the clinical course and causes of mortality increases.

The 12 derivation ECG is one of the most frequently used tests in emergency services, outpatient clinic visits, inpatient wards and intensive care units. Until today, the relationship between the clinical course and mortality of many diseases, especially cardiovascular diseases, and ECG findings has been revealed. Some studies on COVID-19 disease and ECG have been published, and the number of studies demonstrating its relationship with mortality is small, and different parameters were used in each study (6-10). In this study, we wanted to reveal the relationship between ECG parameters and COVID -19

and emphasize the importance of rhythm character and the frontal plane QRS-t angle, which reflects especially the depolarization-repolarization state.

It is emphasized in the updated atrial fibrillation guidelines that the mortality due to all causes is 1.5-3.5 times higher in patients diagnosed with atrial fibrillation, and the presence of AF in addition to those with cardiovascular disease increases mortality and morbidity (11). Among the 259 patients included in the study, 19 patients had a diagnosis of atrial fibrillation. The clinical course of 18 of these patients ended with mortality. In studies conducted with COVID-19 infection, the relationship between AF and mortality has not been emphasized enough, and considering the results of this study, COVID-19 patients with AF may be considered to be at higher risk for mortality.

QT distance is one of the reflections of the ventricular depolarization and repolarization process on the ECG. The relationship between corrected QT (QTc) duration and ventricular arrhythmias and mortality has been demonstrated (12,13). With prolonged QTc, the frequency of ventricular arrhythmias and mortality rate increases especially in cardiovascular diseases. Prolonged QTc duration has been reported to be associated with prognosis in COVID-19 infection (14,15). In our study, the QTc duration was found to be significantly longer in the "deceased patient" group. Considering the results of the study, the prolonged QTc duration may be considered as a mortality predictor in patients diagnosed with COVID-19. In addition, the number of patients with an abnormal QRS axis other than 0-90 degrees is higher in the "deceased patient" group. There was no significant difference between the two groups in terms of the frequency of ventricular premature contraction (VPC). It was concluded that the frequency of VPC does not have a clear effect on mortality in the study population. There was no significant difference between the two groups in terms of PR duration and the frequency of first degree atrioventricular block in the study population. 2nd and 3rd degree atrioventricular block, which is associated with cardiovascular system morbidity and mortality, was not observed in the rhythm records of both groups.

The frontal plane QRS-T angle f (QRS-T), is another ECG parameter that reflects the ventricular deoplarization-repolarization process (16). In previous studies, increased f (QRS-T) angle was found to be associated with mortality in the general population and cardiovascular disease (17-19). In our study, higher f(QRS-T) angle values were observed in the "deceased patient" group compared to the surviving patients. Increased f(QRS-T) angle was thought to be associated with an increased risk of mortality in patients with a diagnosis of COVID-19.

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Considering the demographic characteristics and laboratory results of the study population, there was a higher mean age in the deceased patient group. In previous studies, it was stated that mortality in covid 19 patients increased with increasing age (20,21). Heart failure and history of cerebrovascular disease were statistically significantly higher in the deceased patient group. However, there was no significant difference between the two groups in terms of diseases with high mortality rates such as hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, malignancy and gender. In addition, as acute phase reactants, low albumin, high CRP and ferritin were statistically significant in the deceased patient group, same as results of previous studies (22,23). In our study, as in previous studies, troponin and d-dimer levels were higher in the patient group who died, and their relationship with mortality was also revealed in this study (24,25).

CONCLUSION

Atrial fibrillation, prolonged QTc duration and increased frontal plane QRS-T angle can be considered as mortality predictors in COVID-19 infection, whose mortality rate is high all over the world. We think that patients with these parameters can be evaluated as high-risk and closely monitored from the time of diagnosis, and positive effects on mortality rates can be achieved.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Keçiören Trainig and Research Hospital Clinical Researchs Ethics Committee (Date: 22.12.2020, Decision No: 15/2206).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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