



The effect of the severity COVID-19 infection on electrocardiography

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ABSTRACT

Objective: Acute myocardial damage is detected in a significant portion of patients with coronavirus 2019 disease (COVID-19) infection, with a reported prevalence of 7–28%. The aim of this study was to investigate the relationship between electrocardiographic findings and the indicators of the severity of COVID-19 detected on electrocardiography (ECG).

Methods: A total of 219 patients that were hospitalized due to COVID-19 between April 15 and May 5, 2020 were enrolled in this study. Patients were divided into two groups according to the severity of COVID-19 infection: severe ($n = 95$) and non-severe ($n = 124$). ECG findings at the time of admission were recorded for each patient. Clinical characteristics and laboratory findings were retrieved from electronic medical records.

Results: Mean age was 65.2 ± 13.8 years in the severe group and was 57.9 ± 16.0 years in the non-severe group. ST depression (28% vs. 14%), T-wave inversion (29% vs. 16%), ST-T changes (36% vs. 21%), and the presence of fragmented QRS (fQRS) (17% vs. 7%) were more frequent in the severe group compared to the non-severe group. Multivariate analysis revealed that hypertension (odds ratio [OR]: 2.42, 95% confidence interval [CI]: 1.03–5.67; $p = 0.041$), the severity of COVID-19 infection (OR: 1.87, 95% CI: 1.09–2.65; $p = 0.026$), presence of cardiac injury (OR: 3.32, 95% CI: 1.45–7.60; $p = 0.004$), and d-dimer (OR: 3.60, 95% CI: 1.29–10.06; $p = 0.014$) were independent predictors of ST-T changes on ECG.

Conclusion: ST depression, T-wave inversion, ST-T changes, and the presence of fQRS on admission ECG are closely associated with the severity of COVID-19 infection.

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1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is a disease with high mortality that was named coronavirus disease 2019 (COVID-19) and declared as a global pandemic by the World Health Organization (WHO). The COVID-19 infection may trigger acute cardiovascular events in patients with stable disease or may present with other cardiac complaints including acute coronary syndrome, myocarditis, myopericarditis, acute heart failure, arrhythmia, and sudden cardiac death [1, 2, 3–5]. Cardiac involvement in COVID-19 patients can be demonstrated by various methods such as laboratory techniques (high sensitivity troponin I [hs-TnI], creatine kinase myocardial band [CK-MB], imaging techniques (2-dimensional echocardiography, speckle-tracking echocardiography [STE]), and electrocardiography (ECG).

Hydroxychloroquine and azithromycin are widely used in the treatment and prophylaxis of COVID-19 [6]. Both drugs are known to cause QT interval prolongation and a higher risk of *torsades des pointes* [7,8]. Similarly, lopinavir/ritonavir may lead to QT and PR prolongation. In the case of myocardial injury or acute coronary syndrome that may develop during the follow-up of patients diagnosed with COVID-19, it is important to know the QRS-T morphology in the basal ECG. Therefore, basal ECG taken at the first admission is an important tool for such patients [9]. In addition, the predictors of worse prognosis on ECG in this group of patients have not yet been described. The aim of this study was to investigate baseline ECG parameters and indicators of severity and poor prognosis on ECG in COVID-19 patients.

2. Methods

The study included 219 patients with COVID-19 who underwent ECG at the time of admission between April 10 and 25, 2020 and were found to be positive for COVID-19 on real-time reverse-transcription polymerase chain reaction (RT-PCR) assay. Patients were divided into

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two groups according to the severity of COVID-19 infection: severe ($n = 95$) and non-severe ($n = 124$). Patients with a history of CAD, cardiomyopathy, heart failure, and severe valve disease were excluded from the study. Demographic characteristics including gender, age, smoking, known hyperlipidemia (HLD), hypertension (HT), and diabetes mellitus (DM) were retrieved from medical records. Laboratory parameters including urea, creatinine, sodium, potassium, glucose, hs-TnI, d-dimer, CK-MB, hemoglobin, white blood cell (WBC) count, procalcitonin, and C-reactive protein (CRP) were analyzed from the blood samples taken at the first admission. All patients were above 18 years of age and able to provide a written informed consent, which was a prerequisite for enrollment. The study complies with the Declaration of Helsinki and the trial protocol was approved by the local ethics committee and the Ministry of Health.

2.1. Electrocardiographic evaluation

A 12-lead admission ECG was obtained from each patient before any treatment was started. All standard 12-lead electrocardiograms were recorded on digitized 12-lead ECG recordings using the on-screen digital caliper software (Cardio Calipers version 3.3, Iconico, Inc., New York, NY). All ECGs (filter range 0.5–150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) were analyzed by two independent cardiologists (H.A.B. & A.A.) blinded to the clinical data of the patients according to the modified Minnesota criteria [10] and the findings were recorded on sheets. The ECG findings were examined for the presence of disagreement by another cardiologist (I.S.). In case of disagreements between investigators, a decision was reached by consensus between H.A.B., A.A. & B.G.). The QTc interval, PR interval, and QRS duration were evaluated according to the following criteria: PR interval; normal range 120–200 ms, first-degree atrioventricular block (AVB) was defined as PR interval > 200 ms. QRS duration; lead V5 was selected in all ECG recordings for the measurement of QRS duration, the QRS interval > 120 ms was accepted as prolongation, corrected QT interval (QTc); the QT interval measured in either lead II or V5–6, QTc was calculated using Bazett's formula ($QTc = QT / (\sqrt{RR})$) [11]. Right bundle branch block (RBBB) was defined as broad QRS > 120 ms, RSR' pattern in V1–3 ('M-shaped' QRS complex), wide, slurred S wave in the lateral leads (I, aVL, V5–6). ST-segment depressions were considered to be at least ≥ 0.05 mV in two anatomically contiguous leads, and horizontal and/or downsloping ST depression (in DI, DII, aVL, aVF, V1–V6 derivations) seen after J point. ST elevation was defined as ST-segment elevation at the J point in two contiguous leads of >0.1 mV. T-wave inversion detected as ≥ 0.1 mV and an R/S ratio > 1 in two contiguous leads. ST depression and fQRS myocardial regions on ECG; V1–V4 in the anterior ECG, DI, AVL, V5 and V6 in the lateral ECG, DII, DIII and aVF in the inferior ECG. QRS fragmentation (fQRS) was defined as a notch in the R wave or S wave in two consecutive leads associated with the myocardial region, or multiple R' waves and QRS < 120 ms [12].

According to the WHO interim guidance, the definitive diagnosis of COVID-19 is based on real-time RT-PCR test. In our patients, SARS-CoV-2 RNA was detected by real-time RT-PCR method that was conducted in the Public Health Microbiology Reference Laboratory of the Ministry of Health.

2.2. Definitions

Severe disease was defined in the presence of any of the following criteria: [1] respiratory distress (respiratory rate ≥ 30 breaths per min), [2] oxygen saturation at rest $\leq 93\%$, [3] the ratio of partial pressure of arterial oxygen (PaO₂) to fractional concentration of oxygen in the inspired air (FiO₂) (Pao₂:FiO₂, ≤ 300 mmHg), or [4] critical complications (respiratory failure and requirement of mechanical ventilation, septic shock, and/or multiple organ dysfunction/failure and requirement of

intensive care unit [ICU] admission) [13]. Acute cardiac injury was defined as serum hs-TnI levels above the 99th percentile upper reference limit [14].

2.3. Statistical analysis

All statistical tests were conducted using SPSS for Windows version 19.0 (SPSS Inc., Chicago, IL, USA). Normal distribution of data was assessed using Kolmogorov-Smirnov test. Continuous variables were expressed as mean $\pm$ standard deviation (SD) and categorical variables were expressed as percentages (%). Differences in categorical variables were compared between groups using Fisher's Exact test and/or Chi-square test as needed. Unpaired samples were compared using Student's *t*-test or Mann Whitney *U* test as needed. Independent variables of ST-T change and ICU admission were determined using univariate and multivariate logistic regression analyses. After performing univariate analysis, statistically significant variables were selected into the multivariate logistic regression analysis using the stepwise method. The results of univariate and multivariate regression analyses were presented as odds ratio (OR) with 95% confidence interval (CI). Significance was assumed at a two-sided *p* value of <0.05.

3. Results

Table 1 presents the demographic, clinical, and laboratory parameters of the 219 COVID-19 patients included in the study. No significant difference was found between the severe and non-severe groups in terms of gender while the mean age was significantly higher in the severe group compared to the non-severe group. Of all patients, male patients constituted 64% (61/95) of the severe group and 56% (69/124) of the non-severe group. Mean age was 65.2 ± 13.8 years in the severe group as opposed to 57.9 ± 16.0 years in the non-severe group and a significant difference was established ($p = 0.001$). However, no significant difference was found between the two groups with regard to body mass index (BMI), HT, DM, and HLD. Hemoglobin, WBC, creatinine, sodium, glucose, CRP, procalcitonin, hs-TnI, D-dimer, and CK-MB values were significantly different in the two groups ($p < 0.05$). Mortality

Table 1
Demographic and clinical characteristics

	Severe ($n = 95$)	Non-severe ($n = 124$)	<i>p</i>
Age (years)	65.2 ± 13.8	57.9 ± 16.0	0.001
Male, <i>n</i> (%)	61 (64%)	69 (56%)	0.226
BMI (kg/m ²)	27.3 ± 6.3	26.8 ± 5.4	0.654
Chronic medical illness			
HT, <i>n</i> (%)	51 (53%)	59 (47%)	0.371
DM, <i>n</i> (%)	27 (28%)	39 (31%)	0.628
HLD, <i>n</i> (%)	19 (20%)	17 (13%)	0.213
Laboratory findings at admission			
Hemoglobin (g/dl)	11.5 ± 2.3	12.3 ± 1.6	0.002
WBC (10^3 / μ l)	10.0 ± 4.4	6.7 ± 2.8	<0.001
Creatinine (mg/dl)	0.9 (0.7–1.4)	0.7 (0.6–0.9)	<0.001
Sodium (mmol/L)	136.4 ± 5.8	137.8 ± 3.5	0.031
Potassium (mmol/L)	4.2 ± 0.6	4.3 ± 0.7	0.328
Glucose (mg/dL)	163.4 ± 78.3	121.2 ± 47.8	<0.001
CRP (mg/dL)	106 (57–175)	40 (11–97)	<0.001
Prokalsitonin (ng/mL)	0.38 (0.13–1.44)	0.12 (0.12–0.17)	<0.001
hs-TnI (pg/ml) (NR < 14 pg/ml)	63 (16–225)	6 (3–11)	<0.001
D-dimer (ng/mL)	690 (400–2800)	658 (440–992)	<0.001
CK-MB (ng/mL)	3.2 (1.7–7.0)	1.0 (0.5–1.5)	<0.001
Clinical outcome			
ICU, <i>n</i> (%)	89 (94%)	–	
Non-ICU, <i>n</i> (%)	6 (6%)	124 (100%)	<0.001
MV, <i>n</i> (%)	86 (90%)	–	

Abbreviations: BMI, Body mass index; HT, hypertension; DM, diabetes mellitus; HLD, hyperlipidemia; WBC, white blood cell, CRP, C-reactive protein; hs-TnI, high sensitive Troponin I; CK, creatinine kinase; ICU, intensive care unit; MV, mechanical ventilation.

rates were higher in the severe group compared to the non-severe group (52% vs 7%).

Table 2 presents the comparison of ECG findings between the two groups. The PR interval and QRS duration values were within normal ranges while the heart rate (HR) and QTc interval values were close to the upper limits (HR 91.9 ± 17.9 per minute, PR interval 155.0 ± 23.0 ms, QRS duration 94.5 ± 19.8 , QTc interval 433.5 ± 27.5 ms). In addition, PR depression was detected in 6 (3%), RBBB in 11 (5%), intraventricular conduction delay (IVCD) in 11 (5%), first-degree AVB in 5 (2%), fQRS in 26 (12%), ST-segment depression in 45 (20%), T-wave inversion in 48 (22%), and ST-T changes were detected in 62 (28%) patients.

The HR values were significantly higher in the severe group compared to the non-severe group (95.3 ± 20.0 vs. 89.3 ± 15.8 , $p = 0.019$), while no significant difference was observed in the PR interval, QRS duration, and QTc interval values (155.2 ± 23.0 vs. 154.8 ± 23.0 , $p = 0.907$; 94.8 ± 21.9 vs. 94.2 ± 18.2 , $p = 0.844$; 435.6 ± 33.0 vs. 431.8 ± 22.8 , $p = 0.322$, respectively). Moreover, no significant difference was found between the two groups with regard to the frequencies of RBBB and IVCD, whereas fQRS was more frequent in the severe group compared to the non-severe group ($n = 17$ [17%] vs. $n = 9$ (7%), $p = 0.036$). ST depression, T-wave inversion, and ST-T changes were observed more frequently in the severe group compared to the non-severe group (ST depression, $n = 27$ [28%] vs. $n = 18$ [14%], $p = 0.012$; T-wave inversion $n = 28$ [29%] vs. $n = 20$ [16%], $p = 0.038$; ST-T changes, $n = 35$ [36%] vs. $n = 27$ [21%], $p = 0.016$, respectively).

Patients were also divided into two groups according to the presence of myocardial injury. Myocardial injury was detected in 63 patients and their ECG features were shown in Table 3. No significant difference was found between the patients with and without myocardial injury with

Table 2
Electrocardiographic findings

	All patients (n = 219)	Severe (n = 95)	Non-severe (n = 124)	p
Heart rate, (bpm)	91.9 ± 17.9	95.3 ± 20.0	89.3 ± 15.8	0.019
HR >100 bpm, n (%)	69 (31%)	39 (41%)	30 (24%)	0.008
PVC, n (%)	10 (5%)	3 (3%)	7 (6%)	0.382
PAC, n (%)	9 (4%)	6 (9%)	3 (2%)	0.150
PR interval, (ms)	155.0 ± 23.0	155.2 ± 23.0	154.8 ± 23.0	0.907
PR < 120 ms, n (%)	10 (4%)	4 (5%)	6 (5%)	
PR 120–200 ms, n (%)	184 (84%)	79 (94%)	105 (91%)	
PR > 200 ms, n (%)	5 (2%)	1 (1%)	4 (3%)	
PR depression, n (%)	6 (3%)	3 (3%)	3 (2%)	
QRS duration, (ms)	94.5 ± 19.8	94.8 ± 21.9	94.2 ± 18.2	0.844
QRS > 120 ms, n (%)	32 (14%)	18 (19%)	14 (11%)	0.112
QTc interval (ms)	433.5 ± 27.5	435.6 ± 33.0	431.8 ± 22.8	0.322
QTc > 500 ms, n (%)	12 (5%)	9 (9%)	3 (2%)	0.034
RBBB, n (%)	11 (5%)	3 (3%)	8 (6%)	0.357
IVCD, n (%)	11 (5%)	6 (6%)	5 (4%)	0.538
fQRS, n (%)	26 (12%)	17 (17%)	9 (7%)	0.016
fQRS inferior, n (%)	20 (9%)	14 (14%)	6 (5%)	0.022
fQRS lateral, n (%)	6 (3%)	3 (3%)	3 (2%)	0.981
ST elevation, n (%)	10 (4%)	6 (6%)	4 (3%)	0.150
ST depression, n (%)	45 (20%)	27 (28%)	18 (14%)	0.012
ST depression anterior, n (%)	4 (3%)	0 (0%)	4 (3%)	
ST depression inferior, n (%)	18 (8%)	13 (13%)	5 (4%)	
ST depression lateral, n (%)	20 (9%)	11 (11%)	9 (7%)	
ST depression common, n (%)	3 (2%)	3 (3%)	0 (0%)	
T inversion, n (%)	48 (22%)	28 (29%)	20 (16%)	0.018
T inversion anterior, n (%)	16 (8%)	9 (9%)	7 (6%)	
T inversion inferior, n (%)	12 (5%)	10 (11%)	2 (1%)	
T inversion lateral, n (%)	20 (9%)	9 (9%)	11 (9%)	
ST-T change, n (%)	62 (28%)	35 (36%)	27 (21%)	0.014

Abbreviations: HR, heart rate; PVC, premature ventricular contractions; PAC, premature atrial contraction; QTc, corrected QT; RBBB, right bundle branch block; IVCD, intraventricular conduction delay; fQRS, fragmented QRS.

Data are given as mean $\pm$ SD.

Table 3
Electrocardiographic parameters of patients with and without cardiac injury

	Cardiac injury (+) (n = 63)	Cardiac injury (–) (n = 156)	p
Heart rate, (bpm)	94.3 ± 20.9	90.9 ± 16.6	0.208
PR interval, (ms)	159.6 ± 24.0	153.3 ± 22.4	0.091
QRS duration, (ms)	97.5 ± 26.6	93.2 ± 16.3	<0.001
QRS >120 ms, n (%)	16 (25%)	16 (10%)	0.004
QTc interval, (ms)	438.9 ± 33.9	431.3 ± 24.5	0.067
QTc >500 ms, n (%)	7 (11%)	5 (3%)	0.042
RBBB, n (%)	3 (5%)	8 (5%)	0.911
IVCD, n (%)	6 (9%)	5 (3%)	0.053
fQRS, n (%)	14 (22%)	12 (7%)	0.003
ST depression, n (%)	21 (33%)	24 (15%)	0.003
T inversion, n (%)	24 (38%)	24 (15%)	<0.001
ST-T change, n (%)	31 (49%)	31 (20%)	<0.001

Abbreviations: HR, heart rate; QTc, corrected QT; RBBB, right bundle branch block; IVCD, intraventricular conduction delay; fQRS, fragmented QRS.

Data are given as mean $\pm$ SD.

regard to HR, PR interval, and QTc interval values, while the QRS duration was longer in patients with myocardial injury compared to patients without myocardial injury (97.5 ± 26.6 vs. 93.2 ± 16.3 ms, $p < 0.001$). No significant difference was found between patients with and without myocardial injury with regard to RBBB and IVCD while a significant difference was found with regard to the presence of fQRS ($n = 14$ [22%] vs. $n = 12$ (7%), $p = 0.003$). ST-segment depression, T-wave inversion and ST-T changes were seen more frequently in patients with myocardial injury compared to patients without myocardial injury ($n = 21$ [33%] vs. $n = 24$ [15%], $p = 0.003$; $n = 24$ [38%] vs. $n = 24$ [15%], $p < 0.001$; 31 [49%] vs. 31 [20%], $p < 0.001$, respectively).

Predictors of ST-T segment changes were analyzed by logistic regression analysis (Table 4). In multivariable analysis, presence of HT, severe clinical status, myocardial injury, and d-dimer >500 were determined as predictors of ST-T segment changes (OR: 2.42, $p = 0.041$; OR: 1.87, $p = 0.026$; OR: 3.32, $p = 0.004$; OR: 3.60, $p = 0.014$, respectively).

Predictors of ICU admission were also analyzed by logistic regression analysis (Table 5). In multivariable analysis, age, d-dimer, procalcitonin, myocardial injury, ST depression, and presence of fQRS were revealed as independent predictors of ICU admission (OR: 1.11, $p = 0.014$; OR: 1.95, $p = 0.001$; OR: 1.76, $p = 0.09$; OR: 3.11, $p < 0.001$; OR: 3.42, $p = 0.005$; OR: 1.78, $p = 0.012$, respectively).

4. Discussion

The present study investigated the effect of the severity of COVID-19 infection on the ECG parameters measured at admission and the main

Table 4
Univariate and Multivariate Logistic Regression Analysis on the Risk Factors Associated with ST-T changes in Patients with COVID-19

Variable	Univariate	Multivariate	OR 95% CI	p
OR 95% CI	p	OR 95% CI	p	
Age	1.034	1.013–1.056	0.001	1.025 0.991–1.059 0.148
Gender	1.318	0.727–2.389	0.364	
Hypertension	1.703	0.938–3.092	0.080	2.424 1.035–5.678 0.041
Diabetes mellitus	0.929	0.487–1.771	0.823	
Severe group	2.096	1.154–3.805	0.015	1.872 1.095–2.659 0.026
Creatinine	1.504	1.139–1.987	0.004	1.101 0.747–1.624 0.626
Potassium	0.955	0.667–1.366	0.800	
CRP	1.002	0.999–1.006	0.200	
Hemoglobin	0.968	0.837–1.121	0.665	
Procalcitonin	1.372	1.105–1.704	0.004	1.192 0.934–1.520 0.157
Cardiac injury	4.420	2.227–8.771	<0.001	3.329 1.457–7.609 0.004
D-dimer	2.006	0.943–4.267	0.076	3.608 1.293–10.068 0.014

Abbreviations: HT, hypertension; DM, diabetes mellitus; CRP, C-reactive protein; CK, creatinine kinase, CI: Confidence interval.

Table 5

Univariate and Multivariate Logistic Regression Analysis on the requirement of ICU admission in Patients with COVID-19

Variable	Univariate	Multivariate				
OR	95% CI	p	OR	95% CI	p	
Age	1.241	1.041–1.555	0.003	1.118	1.024–1.278	0.014
Gender	1.510	0.748–2.684	0.614			
Hypertension	1.304	0.848–2.452	0.320			
Diabetes mellitus	1.221	0.677–3.171	0.684			
D-dimer	2.117	1.121–3.398	0.008	1.959	1.121–4.524	0.001
CRP	1.004	0.996–1.013	0.238			
Procalcitonin	1.270	1.075–1.640	0.011	1.762	1.105–2.914	0.009
Cardiac injury	4.195	2.372–9.131	<0.001	3.110	1.887–7.845	<0.001
ST depression	3.124	1.453–6.768	0.007	3.422	1.992–6.972	0.005
fQRS	1.871	1.105–3.841	0.009	1.780	1.095–3.427	0.012

Abbreviations: HT, hypertension; DM, diabetes mellitus; CRP, C-reactive protein; CK, creatinine kinase, CI: Confidence interval.

findings of the study are as follows: i) ST-T changes were the most prevalent ECG abnormality in the severe group, ii) ST depression, T-wave inversion, ST-T changes, and presence of fQRS were more common in the severe group compared to the non-severe group, iii) presence of HT, severe clinical status, myocardial injury and d-dimer elevation were found to be independent predictors of ST-T changes, and iv) age, d-dimer, procalcitonin, myocardial injury, ST depression and presence of fQRS were found to be independent predictors of ICU admission.

Coronavirus disease 2019 (COVID-19) is a pandemic that has affected more than 20 million patients worldwide to date. In many studies, an increased level of troponin, which is a sign of cardiac involvement, has been detected in a significant portion of patients and it has been shown that troponin levels are associated with the severity of the disease and mortality [5,15,16]. Cardiac injury can be measured via biomarkers (such as troponin) under laboratory conditions while it cannot be assessed by invasive procedures (such as biopsy) that can explain the pathophysiology of cardiac involvement due to the risk of infection. Therefore, the use of non-invasive procedures in evaluating cardiac involvement is of paramount importance.

Electrocardiography (ECG) is a commonly used noninvasive test providing rapid results in the evaluation of the cardiovascular system. ECG is an important diagnostic tool used in the assessment of cardiac arrhythmias and myocardial ischemia. Basal ECG is routinely performed before treatment due to the agents used in the treatment of COVID-19 patients. In a study involving 393 patients with COVID-19, atrial arrhythmias were found more frequently in patients requiring mechanical ventilation (17.7% vs. 1.9%) [17]. In Italy, a 60% increase in the rate of out-of-hospital sudden cardiac death was shown during the 2020 COVID-19 pandemic period compared to the same time period of the year 2019 [18]. In a study involving 138 patients that were followed due to COVID-19-related pneumonia in Wuhan, arrhythmias were detected in 17% of all patients and in 44% of the patients hospitalized in ICU [19]. In another study that involved 187 COVID-19 patients, 11% of patients had ventricular tachyarrhythmias at admission [20]. Sinus tachycardia is the most common arrhythmia in COVID-19 patients. In Italy, in a patient who was urgently taken to the catheterization laboratory due to a chest pain and electrocardiographic changes, the patient was diagnosed with COVID-19 while no obstructive CAD was detected [21]. In a case report evaluating the ECGs of two patients with multiple comorbidities, one patient's serial ECG measurements indicated sinus rhythm with first-degree AVB, sinus tachycardia, first-degree AVB with SITIIIQIII, Mobitz type 1 s-degree AVB and atrioventricular junctional escape beat, high-grade AVB or nearly complete AVB with junctional escape rhythm, first-degree AVB, and recovery of SITIIIQIII. In the second patient, serial ECG measurements indicated sinus tachycardia with incomplete RBBB, slightly elevated ST segment, ventricular tachycardia and ventricular fusion, and remarkable ST-segment elevation in the form of triangular QRS-ST-T waveform [22]. In an animal

study examining the effect of coronavirus infection on ECG showed sinus tachycardia, QRS and decreased voltage of T waves, ST-segment changes, and ventricular and occasional supraventricular ectopic beats during the acute phase of rabbit coronavirus infection [23]. In our study, sinus tachycardia was detected in 69 (31%), first-degree AVB in 5 (2%), enlargement of QRS in 32 (14%), extension of >500 ms in QTc in 12 (5%), and ST-T changes were detected in 62 (28%) patients.

In our study, electrical conduction studies indicated RBBB in 5%, IVCD in 5%, and fQRS in 12% of the patients. Fragmented QRS (fQRS) has been identified as a predictor of cardiac events in various disorders, reflecting nonspecific myocardial depolarization. Moreover, fQRS is an electrocardiographic marker of myocardial fibrosis. The prognostic significance of fQRS has mainly been studied in patients with myocardial infarction (MI), ischemic and non-ischemic cardiomyopathies, arrhythmogenic right ventricular dysplasia, and hypertrophic cardiomyopathies [24,25]. In our study, fQRS was found more frequently in the severe group than in the non-severe group, particularly in inferior leads. Similarly, the presence of fQRS was observed more frequently in patients with myocardial injury compared to patients without myocardial injury. The PR interval reflects conduction through the AV node. In our study, PR > 200 ms (first-degree AVB) was observed in 5 (2%) and PR < 120 ms (short PR interval) was detected in 10 (4%) patients.

The QT interval represents the time taken for ventricular depolarization and repolarization. An abnormally prolonged QT (>500 ms) is associated with an increased risk of ventricular arrhythmias, particularly *torsades de pointes*. In a previous multicentric study, 260 (6.1%) out of 4250 patients were diagnosed with COVID-19 and had QTc > 500 ms at admission [26]. However, in another study involving 84 patients taking hydroxychloroquine and azithromycin, baseline QTc was measured as 435 ms before taking these drugs [17]. Advanced age, female gender, diuretic use, hypokalemia, hypomagnesemia, fever, long basal QTc distance (>450 ms), heart failure, ischemia and sepsis, and medications used in treatment are among the risk factors for prolonged QTc interval [27]. In our study, no significant difference was found between the severe and non-severe groups with regard to baseline QTc measurements, whereas QTc > 500 was observed more frequently in the severe patients with myocardial injury.

The ST segment represents the interval between ventricular depolarization and repolarization. Myocardial ischemia or infarction is the most important cause of ST segment abnormality (elevation or depression). ST depression due to subendocardial ischemia may be present in a variable number of leads and with variable morphology. It is often most prominent in the left precordial leads V4–6 plus leads I, II and aVL. The prevalence of ST-T changes in the resting ECG in the Framingham study was found to be 8.5% in men and 7.7% in women and it was reported that the CAD-related morbidity and mortality increased twice in these cases [28]. Myocardial ischemia affects especially the repolarization phase due to intracellular low K⁺ ion, during which action potential times are shortened and the repolarization pattern changes and ST-T changes occur [29]. There have been many studies showing the relationship between ST-T changes and ischemia on ECG, and ST-T changes on ECG have been reported to indicate poor prognosis [30]. ST-T changes are not specific for myocardial ischemia and occur in association with several other disease processes. In a recent study involving a small number of COVID-19 patients, ST segment elevation / ST-T changes were detected in 19.6% of patients, and no association was found with the severity of the disease [31]. In our study, ST depression, T-wave inversion, and ST-T changes were observed more frequently in the severe group than in the non-severe group. Similarly, ST depression, T-wave inversion and ST-T changes were observed more frequently in the group with myocardial injury than in the group without myocardial injury.

The exact cause of ECG changes in patients with COVID-19 remains unknown. However, various possible mechanisms have been proposed for cardiac involvement associated with COVID-19 infection. First, angiotensin-converting enzyme (ACE-II), which is detected at high

concentrations in the heart and lungs, has been defined as a functional receptor for coronaviruses [32]. Myocardial injury due to hypoxemia, myocarditis, microangiopathy, MI, and cytokine storm-related cardiac involvement and injury may have occurred due to systemic inflammatory response [33].

Literature indicates that patients with COVID-19 infection associated with myocardial damage (patients with high troponin), hypoxia, shock (septic or cardiogenic) or patients with widespread systemic inflammation evidence, patients with electrolyte disorder that creates arrhythmia predisposition, patients receiving treatment that could lead to QTc prolongation, and patients with a history of channelopathy (such as Brugada and long QT syndrome) also have an increased risk of arrhythmia [34]. Szekely et al. demonstrated that patients with myocardial injury and worse clinical condition did not have any significant difference in left ventricular (LV) systolic function but had worse right ventricular (RV) systolic function compared to patients with normal troponin or mild clinical condition [35]. Patients receiving treatment that could lead to QTc prolongation and patients with a history of channelopathy (such as Brugada and long QT syndrome) [36] have an increased risk of arrhythmia. Therefore, basal ECG taken at the first admission to hospital is an important tool for these patients [9]. Moreover, basal ECG will provide an evaluation of the ST-T wave in the case of ACS, which may develop during the follow-up of the patient. In addition, the use of chloroquine and azithromycin in the treatment of COVID-19 may cause prolongation in QTc, thereby facilitating the diagnosis of existing channelopathy (such as Brugada and long QT syndrome) along with the measurement of basal QTc interval.

The present study is of high value in that it showed the relationship between ECG measurements obtained at the time of admission and the severity of the disease and cardiac injury in patients diagnosed with COVID-19. The ST depression detected in ECG is a marker of cardiac injury and can be used as an indicator of prognosis in these patients. The COVID-19 patients detected with ischemic (ST-T changes) and arrhythmic parameters (fQRS, QTc prolongation) on basal ECG should be monitored for sudden death risk. In our study, predictors of arrhythmia (e.g. fQRS) and repolarization changes (e.g. ST-T changes) were found to be the independent predictors of cardiac involvement in COVID-19 patients.

In conclusion, ECG findings (ST-T changes, fQRS) are closely associated with the severity of COVID-19. Our study demonstrated that the ECG findings at admission could be used for predicting the presence or absence of myocardial involvement and disease severity. It was also found that cardiac involvement is higher in patients with ST-T changes and fQRS, which may lead to a worse prognosis in such patients.

4.1. Study limitations

Our study had several limitations. First and foremost, it was a single-center study and had a relatively small patient population. Second, no previous ECG recordings of the patients (during their healthy status) were available. Third, no echocardiographic findings were obtained due to the risk of infection transmission.

Author agreement

This statement is to certify that all authors have seen and approved the manuscript.

Being submitted, have contributed significantly to the work, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to the **American Journal of Emergency Medicine**.

We attest that the article is the Authors' original work, has not received prior publication and is not under consideration for publication elsewhere. We adhere to the statement of ethical publishing as appears in the **American Journal of Emergency Medicine**.

On behalf of all Co-Authors, the corresponding Author shall bear full responsibility for the submission. Any changes to the list of authors,

including changes in order, additions or removals will require the submission of a new author agreement form approved and signed by all the original and added submitting authors.

All authors are requested to disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work. If there are no conflicts of interest, the COI should read: "The authors report no relationships that could be construed as a conflict of interest".

Declaration of Competing Interest

None.

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