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The impact of Covid-19 on ECG: A case-control study

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Ethics Committee Approval
The Ethical Review Committee of Harran University, HRU/21.12.19, has approved this study.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Coronavirus Disease 2019 (Covid-19) is a pandemic with fatal effects on the respiratory and cardiovascular systems. Early recognition of complications in the cardiovascular system in Covid-19 disease will guide our treatment management. Therefore, we aimed to examine the changes that occurred in the ECGs of patients with a Covid-19 infection in the last year who were admitted with palpitations.

Methods: Patients who presented to the Cardiology and Internal Medicine outpatient clinics with a complaint of palpitation between June 2021 and July 2021 and who had a Covid-19 infection in the last year were included in this study. A total of 212 patients with a history of Covid-19 and a control group of 185 people without Covid-19 history and cardiac diseases were compared. At admission, QTc, Tp-e interval, frontal QRS-T angle, and fragmented QRS were evaluated on Electrocardiography (ECG).

Results: Among patients with a history of Covid-19 disease, there were 127 (59.91%) males and 85 (40.09%) females. Within the control group, 71 (38.38%) were males and 114 (61.62%) were females. In patients who had a Covid-19 infection, QTc (OR: 1.071, 95% CI: 1.042-1.100, $P<0.001$), frontal QRS-T angle (OR: 1.054, 95% CI: 1.015-1.095, $P=0.007$), and Tp-e interval (OR: 1.253, 95% CI: 1.140-1.377, $P<0.001$) were significantly increased. The difference in fragmented QRS ($P=0.230$) was not significant in logistic regression analysis.

Conclusion: We found increased QTc, Tp-e, and fQRS-T angles in patients who had Covid-19 disease, all of which indicate ventricular repolarization abnormality. Therefore, those with Covid-19 infection should be followed up for malignant arrhythmias.

Keywords: Covid-19, ECG, fQRS-T angle, QTc, Tp-e interval

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Introduction

Coronavirus disease (Covid-19) is defined as "severe acute respiratory syndrome (SARS-CoV-2)" by the World Health Organization [1, 2]. Clinical manifestations range from fever and cough, which are the symptoms of simple respiratory infection, to severe acute respiratory syndrome (ARDS) in Covid -19 infection [3]. Covid-19 can also cause undesirable effects on the heart and cardiovascular system [4], and various clinical conditions such as acute coronary syndrome, myocarditis, arrhythmias, and heart failure were reported [5, 6]. Electrocardiography (ECG) has a vital role in demonstrating cardiac damage and arrhythmic events to explain the clinical changes occurring during Covid-19 infection and give an idea about the problems that may occur in the future. Therefore, the primary aim of our study was to examine the arrhythmic state after cardiac injury, based on ECG findings such as QTc, Tp-e interval, frontal QRS-T angle (fQRS-T), and fragmented QRS (fQRS) in patients who had Covid-19.

Materials and methods

Study design

Patients who visited the Şanlıurfa Mehmet Akif Inan Training and Research Hospital Cardiology Outpatient Clinic and Internal Medicine Outpatient Clinic with complaints of palpitation between June 2021 and July 2021 and who were Covid-19-positive in real-time reverse-transcription (RT-PCR) test within the last year were included in the study. The patients included in the study were divided into two groups. The ECG and laboratory findings of those with a history of Covid-19 in the 1st group (n=212) and those of the healthy population without a history of Covid-19 infection in the 2nd group (n=185) were compared. Patients with ECG abnormalities such as a bundle branch block or atrioventricular block as well as a history of coronary artery disease, previous cerebrovascular event, systolic heart failure, left ventricular hypertrophy, severe heart valve disease, permanent pacemaker, chronic kidney or liver failure, hyperthyroidism, hypertension, pregnancy, electrolyte imbalance were also excluded.

In this prospective study, demographic characteristics, age, gender, hypertension (HT), diabetes mellitus (DM), and smoking history were recorded from the patients' history. Laboratory findings included glucose, urea, creatinine, sodium, potassium, AST, ALT, hemoglobin values, lymphocyte, and neutrophil counts. The Harran University ethics committee approved this study, and written informed consent was obtained from all patients (decree no: HRU/21.12.19).

Electrocardiographic examination

After resting in supine position for 10 minutes, 12-lead ECG recordings were obtained from all cases, with a paper speed of 25 mm per second, a height of 10 mm/mV, and a filter range of 0.16-100 Hz. QT and Tp-e interval measurements were calculated. The QT interval was defined as the distance from the beginning of the Q wave until the end of the T wave. The corrected QT interval (QTc) according to the heart rate was calculated using Bazett's formula. The Tp-e interval was defined as the distance between the peak of the T wave and the endpoint. Tp-e interval measurements were made in the precordial leads [7, 8]. The frontal QRS axis and T-axis were obtained from the automatic report of the ECG device, and these angles were controlled. Frontal QRS-T angle (fQRS-T angle) was defined as the absolute difference between the QRS axis and T-axis (frontal QRST angle = QRS axis – T-axis). When this angle exceeded 180°, the current angle was subtracted from 360° and recalculated [9]. Fragmented QRS was defined as the RSR pattern in at least two consecutive leads and/or the presence of notching in the R and S waves [10].

Statistical analysis

All analyses were performed with SPSS v21 (SPSS Inc. Chicago, Illinois, USA). Shapiro-Wilk test was used to check whether the data were normally distributed. Data were presented as mean (1st quartile – 3rd quartile) for continuous variables and frequency (percentage) for categorical variables. Non-normally distributed variables were analyzed with the Mann-Whitney U test. The Pearson chi-square test was used to assess categorical variables. Logistic regression analysis was performed to determine the risk factors for the presence of Covid 19. Variables that were statistically significant in univariate analyses were included in the regression models. *P*-values of less than 0.05 were considered statistically significant.

Results

The distribution of age, presence of DM, level of ALT was similar among the two groups. Gender, hypertension, smoking, WBC, MPV, neutrophil count, lymphocyte count, monocyte count, platelet count, glucose, potassium, urea, AST, albumin, QT, QTc, fQRS-T angle, and Tp-e interval were related with the presence of Covid-19 (Table 1). The distribution of ECG variables by groups is shown in Figures 1-4.

Figure 1: QT value by groups

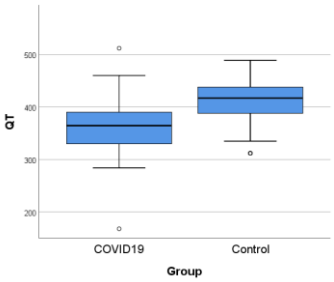


Figure 2: QTc value by groups

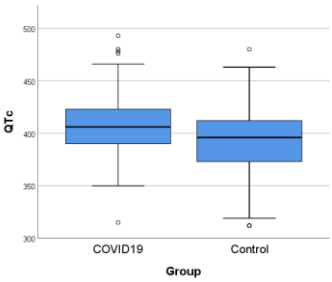


Figure 3: Frontal QRS value by groups

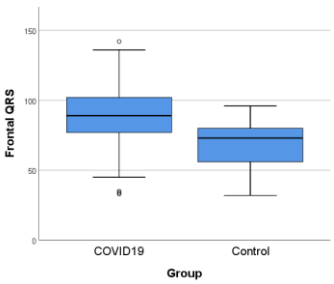
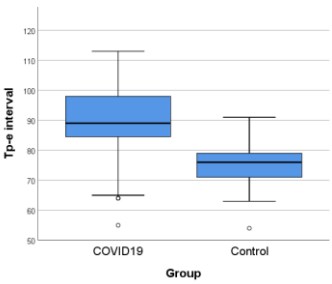


Figure 4: Tp-e interval value by groups



Multiple logistic regression analysis was performed to identify the important factors related to Covid-19. Smoking (OR: 0.182, 95% CI: 0.049-0.675, *P*=0.011), neutrophil count (OR: 1.094, 95% CI: 1.053, 1.138, *P*<0.001), urea level (OR: 1.074, 95% CI: 1.011-1.141, *P*=0.020), AST level (OR: 1.057, 95% CI: 1.003-1.114, *P*=0.040), QT (OR: 0.915, 95% CI: 0.886-0.945, *P*<0.001), QTc (OR: 1.071, 95% CI: 1.042-1.100, *P*<0.001), frontal QRS-T angle (OR: 1.054, 95% CI: 1.015-1.095,

P=0.007), Tp-e interval (OR: 1.253, 95% CI: 1.140-1.377, *P*<0.001) were associated with COVID 19. Other variables included in the sample, such as gender (*P*=0.280), hypertension (*P*=0.304), WBC (*P*=0.142), MPV (*P*=0.686), RDW (*P*=0.404), lymphocyte (0.565), platelet (*P*=0.547), glucose (*P*=0.464), K (*P*=0.727), and fQRS (*P*=0.230) were not (Table 2).

Table 1: Clinical variables by groups

	Group		
	COVID-19	Control	*P*-value
Gender			
Male	127 (59.91%)	71 (38.38%)	<0.001
Female	85 (40.09%)	114 (61.62%)	
Age (years)	54.00 (33.00 - 70.00)	51.00 (44.00 - 57.00)	0.356
DM	51 (24.06%)	34 (19.32%)	0.261
HT	54 (25.47%)	26 (14.29%)	0.006
Smoking	55 (25.94%)	72 (41.11%)	0.001
WBC	8.92 (6.3.00 - 12.00)	8.07 (6.87 - 9.52)	0.010
MPV	10.40 (9.70 - 11.00)	10.50 (9.90 - 11.20)	0.039
RDW	13.20 (12.60 - 14.65)	13.80 (13.00 - 14.50)	0.033
Neutrophils	8.74 (4.17 - 71.00)	4.83 (4.00 - 6.00)	<0.001
Lymphocyte	2.31 (1.51 - 8.00)	2.40 (1.69 - 2.90)	0.034
Monocytes	0.91 (0.56 - 4.20)	0.64 (0.51 - 0.80)	<0.001
Hgb	14.10 (12.35 - 15.25)	13.50 (12.50 - 15.00)	0.143
Hct	42.05 (37.85 - 45.45)	41.10 (38.60 - 45.30)	0.575
Platelet	245.00 (193.50 - 288.50)	268.00 (222.00 - 323.00)	0.001
Glucose	122.50 (102.00 - 177.50)	102.00 (91.90 - 110.20)	<0.001
Sodium	139.00 (136.00 - 141.00)	139.00 (137.00 - 141.00)	0.551
Potassium	4.48 (4.10 - 4.80)	4.29 (4.00 - 4.58)	0.001
Urea	33.00 (24.5 - 44)	27.90 (23.60 - 37.50)	<0.001
Creatinine	0.96 (0.78 - 1.14)	0.82 (0.71 - 0.94)	0.501
ALT	18.85 (11.40 - 30.50)	18.00 (14.50 - 27.50)	0.057
AST	22.65 (16.40 - 33.95)	21.00 (16.00 - 27.00)	<0.001
Albumin	39.27 (32.95 - 44.85)	4.40 (4.00 - 4.60)	<0.001
QT	364.50 (330.00 - 390.00)	417.00 (388.00 - 438.00)	<0.001
QTc	406.00 (390.00 - 423.00)	396.00 (373.00 - 412.00)	<0.001
Fragmented QRS	25 (11.79%)	9 (4.86%)	0.014
Frontal QRS	89.00 (77.00 - 102.00)	73.00 (56.00 - 80.00)	<0.001
Tp-e interval	89.00 (84.50 - 98.00)	76.00 (71.00 - 79.00)	<0.001
Death	23 (10.85%)	0 (0%)	N/A

AST: Alanine Aminotransferase; ALT: Alanine Aminotransferase; QTc: Corrected QT range, DM: Diabetes mellitus, Hgb: Hemoglobin, Hct: Hematocrit, HT: Hypertension, MPV: Mean platelet volume, RDW: Erythrocyte distribution width, WBC: White blood cell count Data were presented as mean (1st quartile – 3rd quartile) for continuous variables and as frequency (percentage) for categorical variables.

Table 2: Key factors of COVID 19, multiple logistic regression analysis

	β coefficient	Standard Error	Wald	*P*-value	Exp(β)	95.0% Confidence Interval for Exp(β)	
Smoking	-1.706	0.67	6.482	0.011	0.182	0.049	0.675
Neutrophils	0.090	0.020	20.949	<0.001	1.094	1.053	1.138
Urea	0.072	0.031	5.411	0.020	1.074	1.011	1.141
AST	0.055	0.027	4.238	0.040	1.057	1.003	1.114
QT	-0.089	0.016	29.253	<0.001	0.915	0.886	0.945
QTc	0.068	0.014	24.696	<0.001	1.071	1.042	1.100
Frontal QRS	0.053	0.019	7.402	0.007	1.054	1.015	1.095
Tp-e interval	0.225	0.048	21.92	<0.001	1.253	1.140	1.377
Continuous	-19.596	5.273	13.812	<0.001	<0.001		

Dependent variables: COVID-19; Nagelkerke R2=0.919

Discussion

This study determined increased QTc, Tp-e interval, and fQRS-T angle, which are vital markers of potentially fatal arrhythmias on surface ECG. The increase in these parameters occurs with the delay in the action potential, which indicates myocardial repolarization. Since ECG is a non-invasive test used to obtain rapid results in evaluating the cardiovascular system, we can also evaluate myocardial repolarization using parameters such as QT interval first and then Tp-e interval and QRS-T angle [11]. As previously known, increased QT and QTc values can result in malignant arrhythmias and sudden cardiac death [12, 13]. Although the measurement of the QT interval and the calculation of the Tp-e interval are not easy, they are unlikely to be repeated. Hence, researchers have started to use the fQRS-T angle, which both shows ventricular repolarization and is automatically calculated by the devices in ECG because of its repeatability [14]. The QRS angle is easily and reproducibly calculated as the difference of the automatically calculated QRS and T-angles in the frontal plane [15]. The fQRS-T angle can be affected by the variables in the action potential. The fQRS-T angle is safer in clinical use compared to the QT interval [16]. Various studies were performed, especially on ventricular repolarization, and a study by Mayet et al. [17] found QTc to be longer in left ventricular hypertrophy (LVH). Using a different method, Zülküf et al. [9] found that the reflection of these parameters, which indicate repolarization, on the ECG significantly increased the fQRS-T angle in patients with LVH. Excluding those with ECG findings suggesting left ventricular hypertrophy in our study renders the increased QTc values more significant. Parameters indicating myocardial repolarization are closely associated with ventricular arrhythmias and mortality [18]. This may cause myocardial damage and subsequent fatal arrhythmias in Covid-19 infection [12]. To the best of our knowledge, there is no study in which QTc, Tp-e, and fQRS-T values are examined together in patients with Covid-19 infection. This study investigated the potential for ventricular repolarization abnormality and arrhythmia with myocardial damage after Covid-19 infection. This finding may be important for the approach to arrhythmias associated with Covid-19. Sinus tachycardia and ST-T changes are observed in most of these patients [19]. Again, Bertini et al. [20] detected atrial fibrillation in 22% of those who had palpitations among those who had Covid-19 infection. The increase in QTc, Tp-e interval, and fQRS-T-angle, which are indicators of myocardial repolarization observed in the ECG in our study, may cause arrhythmic events. Conduction, repolarization abnormalities, and ventricular arrhythmias, including ECG changes such as QTc prolongation, may reflect myocardial injury directly or indirectly associated with Covid-19 pneumonia [21]. fQRS, another parameter examined in our study, reflects non-specific myocardial depolarization and is an indicator of myocardial fibrosis on the ECG. In a study conducted by HA Barman et al., fQRS was observed more frequently in patients who needed intensive care, but this was associated with cardiac damage and mortality [21]. While fQRS was significant in intergroup variables in our study, its absence in multivariate analysis suggests that acute myocardial damage may heal over time or that depolarization abnormality that does not progress to fibrosis is reversible.

Limitations

Although we obtained crucial findings in our study, there are some limitations, some of which are the need for more patients, and the wide age distribution. Also, our control group was not similar to the COVID-19 group regarding gender and smoking frequency distribution, which causes a limitation. However, since both gender and smoking status were stated as risk factors in some literature studies, we did not form the control group in a matched way concerning these factors, and our results were in accordance with the literature in general. In addition, we tried to find out how effective these variables were by performing multivariate analyses. We reduced the likelihood of bias that could occur consequently.

Conclusion

In conclusion, the increase in QTc, Tp-e, and fQRS-T values in those who had Covid-19 infection, especially in those admitted with palpitations, may cause cardiac events that may result in malignant arrhythmias after ventricular repolarization abnormality.

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