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Electrocardiographic Findings of COVID-19 Patients and Their Correlation with Outcome; a Prospective Cohort Study

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Abstract

Introduction: Being infected with COVID-19 is associated with direct and indirect effects on the cardiopulmonary system and electrocardiography can aid in management of patients through rapid and early identification of these adversities.

Objective: The present study was designed aiming to evaluate electrocardiographic changes and their correlation with the outcome of COVID-19 patients.

Methods: This Prospective cohort study was carried out on COVID-19 cases admitted to the emergency department of an educational hospital, during late February and March 2020. Electrocardiographic characteristics of patients and their association with in-hospital mortality were investigated.

Results: One hundred and nineteen cases with the mean age of 60.52±13.45 (range: 29-89) years were studied (65.5% male). Dysrhythmia was detected in 22 (18.4%) cases. T-wave inversion (28.6%), pulmonale P-wave (19.3%), left axis deviation (19.3%), and ST-segment depression (16.8%) were among the most frequently detected electrocardiographic abnormalities, respectively. Twelve (10.1%) cases died. There was a significant correlation between in-hospital mortality and history of diabetes mellitus (p=0.007), quick SOFA score > 2 (p<0.0001), premature ventricular contraction (PVC) (p=0.003), left axis deviation (LAD) (p=0.039), pulmonale P-wave (p<0.001), biphasic P-wave (p<0.001), inverted T-wave (p=0.002), ST-depression (p=0.027), and atrioventricular (AV) node block (p=0.002). Multivariate cox regression showed that history of diabetes mellitus, and presence of PVC and pulmonale P-wave were independent prognostic factors of mortality.

Conclusions: Based on the findings of the present study, 18.4% of COVID-19 patients had presented with some kind of dysrhythmia and in addition to history of diabetes, presence of PVC and pulmonale P-wave were among the independent prognostic factors of mortality in COVID-19 patients.

Key words: Electrocardiography; COVID-19; Heart Diseases; Mortality; Patient Outcome Assessment

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INTRODUCTION

More than 3 months has passed from the emergence of COVID-19 and studies on ways to prevent this disease and treat and improve the outcome of these patients are still ongoing. Cardiometabolic changes and multi-organ dysfunction are among the problems that have been reported following COVID-19 pneumonia. In addition, there are evidence of cardiac involvement and myocarditis in these patients, even in the absence of any sign of pulmonary parenchyma involvement (1). The findings suggest that these adversities worsen the disease and increase the probability of mortality in patients (2-5). On the other hand, underlying cardiovascular disorders have been introduced as a risk factor of mortality among COVID-19 patients and history of cardiovascular diseases is one of the factors that lead to a severe disease (5). Recent studies have shown that after being infected with COVID-19, cardiac disorders are also observed in individuals without a history of cardiac diseases (4). For instance, a recent meta-analysis has shown that the level of troponin I is significantly higher in cases with a severe form of COVID-19 compared to other patients (6). It seems that COVID-19 can directly or indirectly affect the cardiovascular system and lead to myocarditis, myocardial infarction, cardiac

ischemia, arrhythmia and thromboembolism and thus, affect the outcome of the disease (7). However, our knowledge on the cardiac changes that occur following COVID-19 is limited. Therefore, evaluating electrocardiographic changes in these patients could aid in rapid and early detection of cardiac adversities. Additionally, if there is a correlation between electrocardiography changes and outcome of COVID-19, being aware of it can be beneficial in management of infected patients. By reporting 2 cases with COVID-19, Jia He et al. introduced dynamic changes in electrocardiogram (ECG) as an index of cardiac injury and critical status of these patients (8). A study in China reported that around 15.5% of patients with COVID-19 had ECG abnormalities and introduced changes in rate, T wave changes, atrioventricular (AV) node block, and QT changes as the most important observed changes (9). Considering the above-mentioned points, the present prospective cohort study was designed and performed with the aim of evaluating electrocardiographic changes and their correlation with outcome of COVID-19 patients.

Methods

Study design and setting

This Prospective cohort study was carried out on COVID-19 cases admitted to Shohadaye Tajrish Hospital, Tehran, Iran, during late February and March 2020. Electrocardiographic characteristics of patients were investigated and their association with in-hospital mortality was analysed. The study was approved by Ethics Committee of Shahid Beheshti University of Medical Sciences and researchers adhered to ethical practice and confidentiality of patients' information.

Selection of participants

Hospitalized cases with confirmed COVID-19 pneumonia based on chest CT scan and reverse transcription polymerase chain reaction (RT-PCR) were studied. Out of hospital mortality cases, pregnant women, and patients with history of congenital heart disease, as well as multiple trauma patients were excluded.

Data Gathering and outcome

A checklist that consisted of demographic variables (age, sex), comorbidities (hypertension, diabetes mellitus, ischemic heart disease, etc.), presenting vital signs (temperature, blood pressure, heart rate, respiratory rate, and O2 saturation), clinical manifestations, prescribed treatments, ECG variables, and outcomes (discharge, need for mechanical ventilation, and death) was filled out for all included patients. Data gathering and interpretation of ECGs were done by a cardiologist. For mitigating the possible effects of treatment on ECG characteristics (such as QT abnormality), the first ECG of patients obtained at the time of presenting to emergency department was used for interpretations. If an ECG abnormality, such as T wave abnormality, was repeated in at least two leads, the patient was considered positive for that abnormality. All of the 12-lead ECGs were performed with 10 mm (1 mV) amplitude and 25 mm per second speed. Severity of disease was assessed using quick (sequential organ failure assessment score (SOFA score). Based on this score, patients with a score equal to or more than 2 are categorized as high-risk for mortality. The main outcome studied in the present study was in-hospital mortality. All patients were followed up during their hospitalization period. Patients were discharged from the hospital when their chest computed tomography (CT) scan findings were normal and the reverse transcription polymerase chain reaction (RT-PCR) analysis was negative for COVID-19.

Statistical analysis

Analyses were performed using STATA 14.0. The findings were presented as mean ± standard deviation or frequency (%). Cox regression was used to evaluate prognostic factors of mortality in COVID-19 patients. In the first step, using univariate analysis, the relationship between baseline variables and ECG findings with in-hospital mortality was investigated. In the next step, all factors that had a probable relationship with mortality ($p<0.1$) were entered into a multivariate Cox regression model. Also, since previous studies had identified age and sex as risk factors for mortality in COVID-19 patients, the final analyses were adjusted for these two factors. $P<0.05$ was considered as the level of significance.

Results

Characteristics of study subjects

One hundred and nineteen cases with the mean age of 60.52 ± 13.45 (range: 29-89) years were studied (65.5% male). The highest number of patients were in the over 60 years age group. Table 1 shows the baseline characteristics of studied cases. Hypertension (33.4%) and Diabetes mellitus (28.6) were among the most frequent comorbidities among patients. The most frequent clinical symptoms of patients at the time of admission to emergency department were cough (73.1%), dyspnea (71.4%), and fever (53.8%), respectively.

ECG findings

Table 2 shows the detailed ECG findings of studied cases at the time of admission. Thirty-six (30.3%)

Table 1: Baseline characteristics of studied COVID-19 cases

Variable	Value
Sex	
Male	78 (65.5)
Female	41 (34.5)
Age (year)	
20-39	10 (8.4)
40-59	40 (33.6)
≥ 60	69 (58.0)
Comorbidity	
Diabetes mellitus	34 (28.6)
Hypertension	40 (33.4)
Ischemic heart disease	22 (18.5)
Chronic kidney injury	18 (15.1)
Smoking	35 (29.4)
Clinical manifestations	
Fever	64 (53.8)
Cough	87 (73.1)
Dyspnea	85 (71.4)
Nausea	19 (16.0)
Diarrhea	11 (9.2)
Presenting vital signs	
Temperature (°C)	37.43 ± 0.87
SBP (mmHg)	120.68 ± 18.61
DBP (mmHg)	75.14 ± 10.18
Heart rate (/minute)	93.61 ± 19.67
Respiratory rate (/minute)	20.10 ± 3.34
O2 saturation	81.84 ± 9.36

Data are presented as mean ± standard deviation or frequency (%). SBP: systolic blood pressure; DBP: diastolic blood pressure.

cases presented with tachycardia and 2 (1.7%) with bradycardia. Dysrhythmias were detected in 22 (18.4%) cases. T-wave inversion (28.6%), pulmonale P-wave (19.3%), left axis deviation (19.3%), and ST-segment depression (16.8%) were among the most frequent detected ECG abnormalities, respectively.

Outcomes

The mean duration of hospitalization in this series was 7.54 ± 3.40 (range: 1-21) days. 104 (87.4%) cases were discharged from hospital, 16 (13.4%) were intubated and 12 (10.1%) died.

Prognostic factor of Mortality

Univariate analysis showed that there is a significant correlation between in-hospital mortality and history of diabetes mellitus (p=0.007), quick SOFA score > 2 (p<0.0001), premature ventricular contraction (PVC) (p=0.003), left axis deviation (LAD) (p=0.039), pulmonale P-wave (p<0.001), biphasic P wave (p<0.001), inverted T-wave (p=0.002), ST-depression (p=0.027), and AV node block (p=0.002) (Table 2). Mean QT-interval on admission was 413.02±40.95 milliseconds in those who survived and 415.75±16.44 milliseconds in those who did not survive (p = 0.820). Multivariate cox regression showed that history of diabetes mellitus, presence of PVC and pulmonale P-wave were the most important independent prognostic factors of mortality in COVID-19 cases (Table 3).

Table 2: Univariate analysis for assessing the correlation of baseline characteristics and electrocardiogram (ECG) findings with mortality; Data are presented as mean ± standard deviation or frequency (%).

Variable	Alive n=107	Died n=12	Total n=119	p*
Baseline characteristics				
Age (year)	59.8±13.0	67.4±16.0	60.5±13.5	
20-39	9 (8.4)	1 (8.3)	10 (8.4)	0.157
40-59	37 (34.6)	3 (25.0)	40 (33.6)	
≥ 60	61 (57.0)	8(66.7)	69 (58.0)	
Sex				
Male	71 (66.4)	7 (58.3)	78 (65.5)	0.560
Female	36 (33.6)	5 (41.7)	41 (34.4)	
Smoking				
No	78 (72.9)	6 (50.0)	84 (70.6)	0.177
Yes	29 (27.1)	6 (50.0)	35 (29.4)	
Diabetes mellitus				
No	81 (75.7)	4 (33.3)	85 (71.4)	**0.007**
Yes	26 (24.3)	8 (66.7)	34 (28.57)	
Hypertension				
No	73 (68.2)	6 (50.0)	79 (66.4)	0.357
Yes	34 (31.8)	6 (50.0)	40 (33.6)	
Ischemic heart disease				
No	89 (83.2)	8 (66.7)	97 (81.5)	0.239
Yes	18 (16.8)	4 (33.3)	22 (18.5)	
Chronic kidney disease / End-stage renal disease				
No	91 (85.0)	10 (83.3)	101 (84.9)	0.934
Yes	16 (15.0)	2 (16.7)	18 (15.1)	

Table 2 (in continue): Univariate analysis for assessing the correlation of baseline characteristics and electrocardiogram (ECG) findings with mortality; Data are presented as mean ± standard deviation or frequency (%).

Variable	Alive n=107	Died n=12	Total n=119	p*
Quick SOFA score				
0	67 (62.6)	1 (8.3)	68 (57.1)	**<0.001**
1	36 (33.6)	5 (41.7)	41 (34.5)	
2	3 (2.8)	5 (41.7)	8 (6.7)	
3	1 (0.93)	1 (8.3)	2 (1.7)	
ECG findings				
Rate (beat/min)	97.3±21.7	92.0±31.1	96.8±22.7	0.368
Normal	74 (69.2)	7 (58.3)	81 (68.1)	
Tachycardia	32 (29.9)	4 (33.3)	36 (30.2)	
Bradycardia	1 (0.9)	1 (8.3)	2 (2.7)	
Rhythm				
Sinus rhythm	89 (83.2)	9 (75.0)	98 (82.3)	0.586
Atrial tachycardia	3 (2.8)	1 (8.3)	4 (3.4)	0.597
Atrial fibrillation	10 (9.4)	2 (16.7)	12 (10.1)	0.360
Paroxysmal supraventricular tachycardia	5 (4.7)	1 (8.3)	6 (5.0)	0.778
Premature complex				
Premature atrial contraction	13 (12.2)	2 (16.7)	15 (12.6)	0.872
Premature ventricular contraction	15 (14.0)	7 (58.3)	22 (18.5)	**0.003**
Axis deviation				
Right axis deviation	7 (6.5)	1 (8.3)	8 (6.7)	0.768
Left axis deviation	16 (15.0)	5 (41.7)	21 (17.6)	**0.039**
P wave abnormality				
P Pulmonale	15 (14.0)	8 (66.7)	23 (19.3)	**<0.001**
Biphasic P wave	10 (9.4)	6 (50.0)	16 (13.4)	**<0.001**
T wave abnormality				
Tall T wave	2 (1.9)	0 (0.0)	2 (1.7)	>0.999
Inverted T wave	25 (23.4)	9 (75.0)	34 (25.6)	**0.002**
ST segment abnormality				
ST elevation	5 (4.7)	1 (8.3)	6 (5.0)	0.683
ST depression	15 (14.0)	5 (41.7)	20 (16.8)	**0.027**
Blocks				
Right bundle branch block	6 (5.6)	1 (8.3)	7 (5.9)	0.928
Left bundle branch block	5 (4.7)	2 (16.7)	7 (5.9)	0.063
Atrioventricular node block	0 (0.0)	1 (8.3)	1 (0.84)	**0.002**
Sinus arrest	3 (5.0)	0 (0.0)	3 (4.5)	>0.999
Intervals				
PR prolongation (≥ 20ms)	21 (19.6)	5 (41.7)	26 (21.8)	0.132
QTc day 1 (≥ 440ms)	28 (26.2)	1 (8.3)	29 (24.4)	0.289

*Based on univariate cox regression. Bold values are significant.

Table 3: Multivariate cox regression for assessing the correlation of baseline characteristics and electrocardiogram findings with mortality

Variable	Hazard ratio	95% confidence interval	P
Age	0.98	0.90-1.06	0.555
Male sex	4.52	0.80-25.40	0.089
Diabetes mellitus	56.87	2.58-1254.28	**0.010**
Quick SOFA score≥2	1.34	0.24-7.37	0.734
Premature ventricular contraction	18.44	2.20-154.30	**0.007**
Left axis deviation	0.90	0.05-15.97	0.950
P pulmonale	17.63	1.59-195.22	**0.019**
Biphasic P wave	1.24	0.11-13.66	0.862
Inverted P wave	7.44	0.73-73.36	0.089
ST depression	1.65	0.22-12.21	0.625
Left bundle branch block	2.91	0.07-113.93	0.568
Atrioventricular node block	1.58	0.013-187.39	0.852

Bold values are significant.

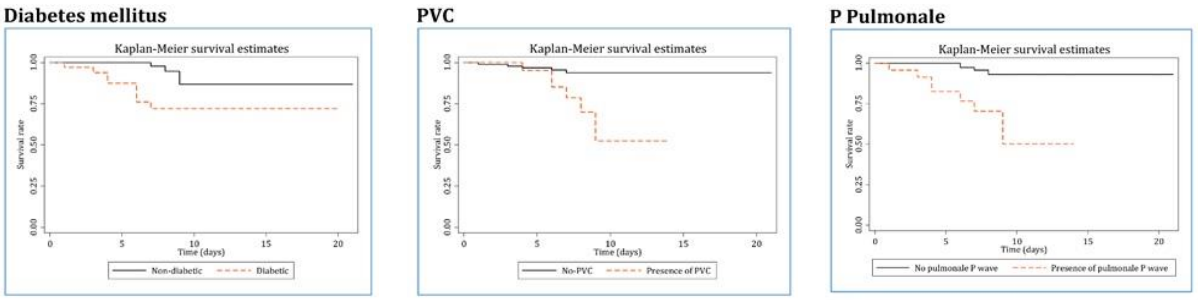

Figure 1: Kaplan-Meier survival graph for independent prognostic factors of COVID-19 mortality

Table 4: Correlation between presence of independent prognostic factors and mortality of COVID-19 patients

Number of prognostic factor(s)	Alive	Dead
0	57 (100.0)	0 (0.0)
1	44 (95.6)	2 (4.4)
2	6 (40.0)	9 (60.0)
3	0 (0.0)	1 (100.0)

Prognostic factors included diabetes mellitus, premature ventricular contraction (PVC), and P Pulmonale

Kaplan-Meier survival graph for independent prognostic factors of COVID-19 mortality is presented in figure 1. Among the 12 patients who died, 2 (16.6%) had one prognostic factor, 9 (75.0%) had two prognostic factors and 1 (8.3%) patient had 3 prognostic factors (table 4).

Discussion

Based on the findings of the present study, 18.4% of patients with COVID-19 had presented with some kind of dysrhythmia and in addition to diabetes mellitus, presence of PVC and pulmonale p wave were among the independent prognostic factors of mortality in COVID-19 patients. Presence of pulmonale P wave is a consequence of increased pulmonary vascular resistance and right atrial dilatation (10). Increase in pulmonary vascular resistance can be either chronic or acute. Underlying pulmonary diseases and chronic obstructive pulmonary disease (COPD) are among the chronic causes of increase in pulmonary vascular resistance and formation of pulmonale P wave. On the other hand, ailments such as pulmonary embolism can acutely cause pulmonale P wave formation in the ECG. In other words, when an embolism is formed we will witness a right heart strain and acute cor pulmonale (11). There are studies that have reported a rise in the risk of pulmonary embolism following infection with COVID-19 (12, 13). The reason for this might be the high affinity of the COVID-19 virus to vascular endothelium, causing endothelial injury and paving the way for thrombosis (14). Additionally, some studies have shown that right atrial enlargement is one of the most important prognostic factors of mortality in pulmonary embolism patients with stable hemodynamics (15, 16). Whatever the cause for formation of pulmonale P wave, the situation is dangerous in nature for the affected patients. The present study shows that presence of PVC in ECG of COVID-19 patients on admission is associated with increased risk of mortality. Presence of PVC alone may indicate ischemia, ischemic cardiac dysfunction, and low cardiac reserve. Existing evidence show that myocardial infarction, myocarditis, and acute coronary syndrome are the most commonly observed disorders following COVID-19 infection (7). Presence of PVC can either be an underlying cardiac problem for the patient or can be caused as a direct or indirect effect of COVID-19 infection on the cardiovascular system. In a meta-analysis on the data of 4 original articles, which included the data of 341 patients, it was revealed that mean serum level of cardiac troponin I was significantly higher in patients with severe cases of COVID-19 compared to non-severe cases (6). Four cohort studies on hospitalized COVID-19 patients in China showed that the rate of cardiac complications in hospitalized patients varies from 7% to 17%. These studies showed that the prevalence of cardiac disorders in intensive care unit (ICU) admitted patients was 22.2%, while this rate was 2% in other patients. The interesting point is that the rate of cardiac disorders has been reported to be as high as 59% in patients who died, but about 1% in other patients (17-20). Therefore, whether PVC is a manifestation of the patient's previous cardiac problems or a disorder caused by direct or indirect effects of COVID-19 on the cardiovascular system, its presence can be considered as an independent risk factor for mortality. Diabetes is another prognostic factor, which is associated with increased risk of mortality among patients. Diabetes is one of the most common comorbidities among COVID-19 patients (21). In the present study, diabetes was a

prognostic factor for mortality, while in the study by Zhou et al. it had no correlation with mortality of patients (22). The reason for this difference could be the retrospective design of the study by Zhou et al. as well as differences between the Iranian and Chinese populations. Meanwhile, in another study on 1590 patients, a significant correlation was found between diabetes and undesirable outcome in COVID-19 patients (23). One of the probable mechanisms suggested for the relationship between COVID-19 and diabetes is the interaction of the virus with angiotensin-converting enzyme 2, which is expressed in epithelial and vascular cells. It seems that diabetes leads to an increase in the expression of proteins in this pathway, which exacerbates the condition of the patient (21). However, this proposed mechanism has been challenged recently and there are doubts about it (24). Another mechanism that can be considered for diabetes in exacerbation of COVID-19 patients' condition is its correlation with pulmonary embolism. Diabetes is one of the known risk factors of pulmonary embolism (22, 25). Presence of diabetes in COVID-19 patients can be a predisposing factor for pulmonary embolism and formation of numerous micro-emboli in pulmonary vessels. However, further studies are needed for confirming this hypothesis. One of the important points that should be considered regarding ECG changes in patients with COVID-19 is the QTc interval. We currently know that one of the side effects caused by commonly used drugs for treating these patients, i.e. hydroxychloroquine and some antiviral drugs, is increasing the QT interval. Since this can set the stage for formation of lethal dysrhythmia such as torsade de pointes and ventricular tachycardia, patients, especially those who have been hospitalized, should be monitored in this regard.

Limitations

One of the limitations of the present study was its relatively small sample size. However, it should be noted that the present study is one of the few prospective studies performed on COVID-19 regarding ECG changes. In addition, in order to reach a more accurate conclusion regarding the weight of ECG findings in predicting the outcome of patients, a more comprehensive study including other known risk factors of death in these patients should better be performed so that more accurate data can be found. Another limitation of this study was using quick SOFA score instead of more accurate scales of disease severity. Severity of disease had better been evaluated using more accurate scales such as APACHE; however, considering the critical conditions of the hospital and the treatment team this could not be done.

Conclusions

Findings of the present study showed that evaluating ECG changes could provide the treatment team with good information on the patient's prognosis. Considering the findings of the present study, it seems that ECG changes in patients presenting with COVID-19, whether they indicate underlying cardiac illnesses or are side effects of the infection, can affect the outcome of patients. Therefore, in times of doubt about managing the patient as an in-patient or an out-patient, or when triage is required for allocation of equipment to more critical patients, considering ECG findings may help in selecting patients with higher risks. Based on the findings of the present study, 18.4% of COVID-19 patients had presented with some kind of dysrhythmia and in addition to history of diabetes, presence of PVC and pulmonale p wave were among the independent prognostic factors for mortality of COVID-19 patients.

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Authors' contribution

Study design: Mehdi Pishgahi, Mahmoud Yousefifard, Saeed Safari; Data gathering: Mehdi Pishgahi; Analysis: Mahmoud Yousefifard; Interpretation of results: All authors; Drafting: Mahmoud Yousefifard, Saeed Safari; Critically revised: All authors.

Conflict of interest

None declared.

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