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Observational Study

Conduction system disorders and electro-cardiographic findings in COVID-19 deceased patients in 2021, Shiraz, Iran

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Abstract

BACKGROUND

Cardiac conduction disorders and electrocardiographic (ECG) changes may occur as a manifestation of coronavirus disease 2019 (COVID-19), especially in severe cases.

AIM

To describe conduction system disorders and their association with other electrocardiographic parameters in patients who died of COVID-19.

METHODS

In this cross-sectional study, electrocardiographic and clinical data of 432 patients who expired from COVID-19 between August 1st, 2021, and December 1st, 2021, in a tertiary hospital were reviewed.

RESULTS

Among 432 patients who died from COVID-19, atrioventricular block (AVB) was found in 40 (9.3%). Among these 40 patients, 28 (6.5%) suffered from 1st degree AVB, and 12 (2.8%) suffered from complete heart block (CHB). Changes in ST-T wave, compatible with myocardial infarction or localized myocarditis, appeared in 189 (59.0%). Findings compatible with myocardial injury, such as fragmented QRS and prolonged QTc, were found in 91 patients (21.1%) and 28 patients (6.5%),

respectively. In patients who died of COVID-19, conduction disorder was unrelated to any underlying medical condition. Fragmented QRS, axis deviation, and ST-T changes were significantly related to conduction system disorder in patients who died of COVID-19 (P value < 0.05).

CONCLUSION

Conduction system disorders are associated with several other ECG abnormalities, especially those indicative of myocardial ischemia or inflammation. Most patients (73.14%) who died of COVID-19 demonstrated at least one ECG abnormality parameter. Since a COVID-19 patient's ECG gives important information regarding their cardiac health, our findings can help develop a risk stratification method for at-risk COVID-19 patients in future studies.

Key Words: COVID-19; Conduction system disorder; Electrocardiography; Atrioventricular block

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Core Tip: No study has yet transpired to assess the correlation of conduction system disorders with other electrocardiographic findings in the setting of coronavirus disease 2019 (COVID-19). This paper can shed light on different conduction disorders seen in COVID-19.

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INTRODUCTION

In December 2019, a cluster of pneumonia cases was reported in Wuhan, Hubei Province, China, caused by a novel coronavirus. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) triggered the respiratory infection coronavirus disease 2019 (COVID-19). Due to the rapid transmission of COVID-19, WHO declared a pandemic on March 11th, 2020[1].

The initial studies of COVID-19 considered it to be predominantly a respiratory disease. However, recent evidence highlights multiple organ system involvements in COVID-19, including coagulation system disorder, acute kidney injury, hepatocellular injury, and cardiac and central nervous system complications[2]. The cardiac complications include thromboembolic events, heart failure, heart block, acute coronary syndrome, myocarditis, arrhythmias, and sudden cardiac death[3,4].

More recently, a growing body of literature on COVID-19 has investigated the electrophysiological changes that arise as a clinical manifestation of COVID-19 and highlighted the variety of arrhythmias observed in patients with COVID-19[5]. Moreover, multiple case reports introduce atrioventricular block as a potential manifestation of COVID-19[6-14]. In a retrospective study about the prognostic significance of electrocardiographic (ECG) findings in 319 patients with COVID-19, T-wave change (31.7%), QTc interval prolongation (30.1%), and arrhythmias (16.3%) were three most common found ECG abnormalities and atrioventricular block was presented in 3.9% of the patients[15]. First-degree atrioventricular block (AVB) was seen in 10 patients (3.3%), and second-degree AVB Mobitz type I was found in 2 patients (0.7%). In-hospital mortality risk increased with increasing abnormal ECG parameters[15]. In another study investigating the association between electrocardiographic features and mortality in COVID-19 patients, the overall prevalence of AVB was 11.8%, with deceased patients showing higher incidence than recovered patients (25% vs 9%)[16]. Another study conducted a rigorous patient-level analysis to determine the association of acute malignant cardiac arrhythmias, such as tachy- or bradyarrhythmias, and mortality in 140 hospitalized patients with COVID-19 and AVB was found in 5 patients, 2 of whom were associated with myocardial infarction (MI), and another 2 had metabolic abnormalities, suggesting that refractory shock was primarily responsible for conduction block, and the remaining patient had AVB in the setting of non-ST-segment-elevation myocardial infarction and newly diminished left ventricular ejection fraction[17]. However, no association between the presence of AVB and mortality was reported in these studies. Finally, it is evident that the knowledge of electrophysiological abnormalities, conduction system disorder, and particularly atrioventricular blocks is largely based on very limited data.

We designed the present study to investigate whether disruption of the conduction system can herald other ECG abnormalities in the setting of COVID-19, and whether it is associated with underlying diseases.

MATERIALS AND METHODS

This is a cross-sectional descriptive study that retrospectively reviewed deceased COVID-19 patients who were admitted to Faghihi Hospital of Shiraz University of Medical Sciences from August 1st until December 1st, 2021. The inclusion criteria were all the admitted patients aged 18 or older who died with the diagnosis of COVID-19. Faghihi Hospital, located in Shiraz, Fars Province, Southern Iran, is one of the major tertiary teaching hospitals responsible for treating COVID-19 patients.

Data collection

Electronic demographic and on-paper medical records were evaluated. The data was gathered into a planned-out questionnaire. The questionnaire included demographic data, underlying diseases, and ECG factors. The data were collected by six independent practitioners. ECGs were interpreted by two cardiologists blinded to the patients' information and confirmed by an electrophysiologist.

Basic ECG parameters (rhythm, rate, axis, and ventricular hypertrophy), new findings attributable to COVID-19 (ST elevation and atrioventricular conductance disturbances), repolarization variants (J elevation, early repolarization, Brugada pattern, U wave, QTc prolongation, QT dispersion (QTd), the slope of terminal part of T wave (T-slope), depolarization abnormalities BBBs, low voltage QRS, poor R wave progression, and fragmented QRS (fQRS), QRS duration prolongation), and ECG pulmonary patterns such as S1Q3T3 were evaluated and recorded. Conduction system disorders were defined as BBBs and AVBs, and their coincidence with other ECG abnormalities was evaluated.

All ECGs were taken by the hospital's employed and trained technicians who were blinded to the purpose of the study and the patient's medical information using "Electrocardiogram Dena650" produced by SAADAT Company, Tehran, Iran.

COVID-19 was confirmed in these patients by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA detection with nasal and pharyngeal swabs, performed at admission or during hospitalization.

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 19.0 (IBM corp.) for windows. Categorical variables were shown as frequency and percentages, and continuous variables as mean \pm SD. Chi-square test was performed to assess the relationships between ECG parameters and patients' medical conditions with conduction system disease. The presence of conduction system disorders was considered the outcome variable, and ECG parameters were regarded as dependent variables. Then, the association of conduction system disorders and ECG parameters was calculated using logistic regression, and adjusted odds ratios were reported for univariate analysis and multivariate analysis after adjustment for the presence of other ECG parameters, sex, age, and underlying diseases. A two-sided *P* value less than 0.05 was considered statistically significant.

RESULTS

Among the 432 deceased patients, 261 (60.4%) were male, with a mean age of 67.02 (\pm 14.44) years and age range of 28 - 96. The most prevalent comorbid diseases were hypertension (47.9%/207 cases), diabetes mellitus (36.3%/157 cases) and cardiac diseases (35.2%/158 cases). The prevalence of other comorbidities in order of frequency is as follows: coronary disease (18.5%/80 cases), hyperlipidemia (12.5%/54 cases), pulmonary disease (8.6%/37 cases), and chronic kidney disease (6.3/27 cases). Evaluating the association between patients' past medical conditions and conduction system disorders in patients who died of COVID-19 revealed that conduction disorders were not related to any underlying medical condition. A summary of demographic and comorbid diseases is shown in [Table 1](#).

Regarding heart rate and rhythm, sinus tachycardia (HR > 100) and bradycardia (HR < 60) were noticed in 100 (23.1%) and 9 (2.3%) patients, respectively. Abnormal rhythms were noted in 66 (15.2%) patients. The most prevalent arrhythmia was atrial fibrillation (12.5%). Reviewing electrocardiographic findings, AVB was found in 40 (9.3%) patients. 28 (6.5%) of the patients suffered from 1st degree AVB, and 12 (2.8%) suffered from CHB. Changes in ST-T wave compatible with myocardial infarction or localized myocarditis appeared in 189 (59.0%) patients. Other abnormal conduction system findings were bundle branch blocks. Left bundle branch block was seen in 25 (5.8%) patients, and right bundle branch block was seen in 50 (11.6%) patients. Moreover, the prevalence of findings compatible with pulmonary diseases such as S1Q3T3, poor R progression, axis deviations, and low voltage ECG was 14.4% (62 patients), 41.0% (177 patients), 21.7% (94 patients), and 11.3 (49 patients), respectively.

Table 1 Association of patients' past medical conditions and conduction system disorder in coronavirus disease 2019 deceased patients

Medical condition		Patients without conduction system disorder (n = 317)	Patients with conduction system disorder (n = 108)	P value
Sex	Female	125 (73.1)	46 (26.9)	0.654
	Male	196 (75.1)	65 (24.9)	
Age, yr	≤ 50	46 (79.3)	12 (20.7)	0.147
	51-60	65 (81.3)	15 (18.8)	
	61-70	82 (75.2)	27 (24.8)	
	> 70	128 (69.2)	57 (30.8)	
IHD	Yes	57 (71.3)	23 (28.8)	0.477
	No	260 (75.4)	85 (24.6)	
DM	Yes	113 (72.0)	44 (28.0)	0.357
	No	204 (76.1)	64 (23.9)	
Renal disease	Yes	42 (79.2)	11 (20.8)	0.501
	No	275 (73.9)	97 (26.1)	
Pulmonary disease	Yes	23 (62.2)	14 (37.8)	0.078
	No	292 (75.6)	94 (24.4)	
Hyperlipidemia	Yes	38 (70.4)	16 (29.6)	0.503
	No	279 (75.2)	92 (24.8)	
CKD	Yes	19 (70.4)	8 (29.6)	0.648
	No	298 (74.9)	100 (25.1)	
HTN	Yes	151 (72.9)	56 (27.1)	0.504
	No	165 (76.0)	52 (24.0)	

IHD: Ischemic heart disease; DM: Diabetes mellitus; CKD: Chronic kidney disease; HTN: Hypertension.

Findings compatible with myocardial injury, such as fragmented QRS, and prolonged QTc, were assessed, with a prevalence of 21.1% (91 patients), and 6.5% (28 patients). Primary electrical cardiac diseases such as prominent J wave, Brugada pattern, and early repolarization were observed in 4.4% (19 patients), 1.2% (5 patients), and 4.2% (18 patients), respectively.

Regarding ECG parameters in patients who died of COVID-19, in univariate analysis, ST-T changes, fragmented QRS, axis deviation, presence of S1Q3T3, and poor R wave progression were significantly related to conduction system disorders in patients who died of COVID-19 (P value < 0.05, Table 2). However, when adjusted for age, sex, underlying diseases, and other ECG parameters, only fragmented QRS, ST-T changes, and axis deviation were significantly associated with conduction system disorders.

DISCUSSION

This is a single-center study conducted retrospectively. The small sample size of a single-center could result in less generalizability. Unfortunately, assessing the presence of myocarditis was not possible due to the absence of data on serum markers and echocardiographic examination for most of our enrolled patients. This descriptive study aims only to report the incidence of ECG abnormalities and their relationship with conduction system disorders in patients who died of COVID-19. To determine which conduction disorders are independently associated with mortality, case-control or cohort studies are recommended.

By reviewing previous literature, mounting evidence supports the association between influenza pneumonia and heart diseases, and it has been reported that influenza have been associated with a six-fold increased risk of acute MI[18,19]. COVID-19 also directly and indirectly affects the cardiovascular system and the heart in particular[3]. Previous studies have proved that COVID-19 augments the risk of cardiovascular complications, including dysrhythmias, both in the short and long term, and given that

Table 2 Electrocardiographic parameters in conduction system disease in COVID-19 deceased patients

ECG parameters		Patients without conduction system disorder (n = 317)	Patients with conduction system disorder (n = 108)	Univariate OR (95%CI for OR)	P value	Adjusted ¹ odds ratio (95%CI for OR)	P value
Fragmented QRS	Yes	53 (58.2)	38 (41.8)	2.63 (1.61-4.30)	< 0.001	2.27 (1.23, 4.16)	0.008
	No	268 (78.6)	73 (21.4)	1	-	1	-
ST-T change	Yes	125 (66.1)	64 (33.9)	2.14 (1.38-3.31)	0.001	1.81 (1.07, 3.08)	0.030
	No	196 (80.7)	47 (19.3)	1	-	1	-
Rhythm	Sinus rhythm	279 (76.2)	87 (23.8)	1	-	1	-
	AF	34 (63.0)	20 (37.0)	1.89 (1.03-3.45)	0.039	1.70 (0.78-3.71)	0.179
	Others	8 (66.7)	4 (33.3)	1.60 (0.47-5.45)	0.450	0.75 (0.15, 3.62)	0.700
Rate	Bradycardia (HR < 60)	5 (55.6)	4 (44.4)	2.10 (0.55-8.01)	0.279	1.67 (0.31-9.06)	0.554
	Normal (60 < HR < 100)	234 (72.4)	89 (27.6)	1	-	1	-
	Tachycardia (HR > 100)	82 (82.0)	18 (18.0)	0.58 (0.33-1.02)	0.057	0.55 (0.27, 1.09)	0.086
Axis deviation	Normal	283 (83.7)	55 (16.3)	1	-	1	-
	Left	14 (48.3)	15 (51.7)	5.51 (2.52-12.07)	< 0.001	3.74 (1.50-9.33)	0.005
	Right	24 (36.9)	41 (63.1)	8.79 (4.92-15.71)	< 0.001	7.67 (3.95-14.88)	< 0.001
QTc 1	< 500	211 (75.1)	70 (24.9)	1	-	1	-
	> 500	110 (73.3)	40 (26.7)	1.10 (0.70-1.72)	0.691	0.94 (0.53, 1.66)	0.819
QTc 2	Male ≤ 440 and female ≤ 460	300 (74.4)	103 (25.6)	1	-	Not included due to collinearity with the above variable	
	Male > 440 and female > 460	21 (75.0)	9 (25.0)	0.97 (0.40-2.35)	0.948		
QTd	< 40	45 (81.8)	10 (18.2)	1	-	1	-
	≥ 40	276 (73.2)	101 (26.8)	1.65 (0.80-3.39)	0.176	1.42 (0.58-3.47)	0.446
J wave	Yes	13 (68.4)	6 (31.6)	1.35 (0.50-3.65)	0.550	0.98 (0.28-3.49)	0.978
	No	308 (74.6)	105 (25.4)	1	-	1	-
U wave	Yes	32 (71.1)	13 (28.9)	1.20 (0.60-2.38)	0.605	1.10 (0.47, 2.63)	0.815
	No	289 (74.7)	98 (25.3)	1	-	1	-
Early repolarization	Yes	15 (83.3)	108 (26.1)	0.57 (0.16-2.00)	0.377	1.00 (0.26-3.93)	0.998
	No	306 (73.9)	108 (26.1)	1	-	1	-
T slope	< 30	12 (75.0)	4 (25.0)	1	-	1	-
	30-60	302 (74.6)	103 (25.4)	1.02 (0.32-3.24)	0.969	0.79 (0.21, 2.98)	0.728
	> 60	7 (63.6)	4 (36.4)	1.71 (0.32-9.11)	0.527	1.87 (0.249-14.01)	0.551
SIQ3T3	Yes	38 (61.3)	24 (38.7)	2.05 (1.17-3.61)	0.012	1.83 (0.92-3.64)	0.086
	No	283 (76.5)	87 (23.5)	1	-	1	-
Low voltage QRS	Yes	42 (85.7)	7 (14.3)	0.45 (0.20-1.03)	0.058	0.38 (0.14-1.05)	0.063
	No	279 (72.8)	104 (27.2)	1	-	1	-
PRP	Yes	121 (68.4)	56 (31.6)	1.68 (1.09-2.60)	0.019	1.32 (0.77-2.26)	0.317
	No	200 (78.4)	55 (21.6)	1	-	1	-

¹Adjusted for age, sex, underlying diseases, and other electrocardiography findings.

AF: Atrial fibrillation; HR: Heart rate; QTc: Corrected Q-T interval; QTd: Q-T interval dispersion; T slope: T-wave terminal slope; PRP: Poor R wave progression.

they are the most prevalent viral pneumonia at the time of writing this article, their complications impose a considerable burden on healthcare[20]. This study discusses the prevalence of arrhythmias and conduction system disorders in patients with COVID-19.

The mechanism underlying the development of arrhythmias in COVID-19 has not been specified. However, potential triggers are as follows[21]. First, electrolyte imbalance caused by COVID-19 symptoms such as diarrhea and complications such as acute kidney injury or severe sepsis is a notable cause[22]. Second, SARS-CoV-2-induced myocardial injury due to the upregulation of angiotensin-converting enzyme 2 (ACE2) receptor during viral invasion and severe hypoxia-induced myocyte necrosis are other potential causes of arrhythmias[23]. In addition, acute myocardial infarction due to demand/supply imbalance and arterial thrombotic events secondary to hypercoagulable state can cause acute arrhythmias[24,25]. Stress and cytokine storm in relation to sepsis and high inflammatory state is another potential mechanism[21]. Moreover, prolonged QTc-induced malignant ventricular arrhythmias and channelopathies induced by off-label medical therapy and antiviral therapy could be introduced as direct triggers of arrhythmias[26].

The most remarkable result acquired from the data was the prevalence of advanced AVB in patients who died of COVID-19. This prevalence was not yet assessed in deceased COVID-19 patients; however, the reported prevalence of AVB in COVID-19 patients ranged from 3 to 12% in different studies[14,15]. All types of AVBs were seen in 40 (9.3%) cases in our study. Among those with AVB, 12 (2.8%) cases suffered from 3rd degree complete heart block (CHB). CHB has been assumed to be a rare ECG feature of COVID-19, and this novel finding has only been reported in a few case studies[6,8,10].

Another interesting result was the high prevalence of fragmented QRS, prominent J wave, and ST-T wave change. These parameters can be directly related to myocardial injury induced by SARS-CoV-2 infection. In addition, the high incidence of S1Q3T3 and LBBB in this study could indicate pulmonary involvement in deceased COVID-19 cases. S1Q3T3 is a relatively specific pattern for pulmonary thromboembolism and a potential cause of death[27].

Moreover, ST-T changes, fragmented QRS, and axis deviation were significantly related to conduction disorders in our patients, suggestive of new-onset myocardial infarctions during the infection and increased mortality risk. Our study provides further evidence for the observed ST-T wave changes in COVID-19 patients, suggestive of myocardial infarction or localized myocarditis[28]. This indicates that disturbances in the conduction system are associated with COVID-19-related myocardial injury, either ischemic or inflammatory.

Compatible with previous studies, atrial fibrillation was the most prevalent arrhythmia[29]. It is notable that we witnessed these findings in patients who had no evidence of arrhythmia before their admission. Therefore, we suggest future studies to focus on the mechanism of arrhythmogenicity of COVID-19 and discover the proper screening and therapeutic strategies mitigating the adverse outcomes of COVID-19-induced arrhythmias.

CONCLUSION

To the best of our knowledge, this is the first study that exclusively assessed expired COVID-19 patients and illuminated the AVB and BBB prevalence among them. The myocardial injury appears to be closely associated with conduction system disorders and has a role in COVID-19 morbidity and mortality. Our findings can help develop a risk stratification method for susceptible COVID-19 patients in future studies. Consequently, we recommend that health policymakers should consider separate catheterization laboratories that provide service only to COVID-19 patients.

ARTICLE HIGHLIGHTS

Research background

Coronavirus disease 2019 (COVID-19) is associated with a wide range of cardiovascular complications, especially in severe cases. Electrocardiogram is a cheap, useful and readily available tool to investigate these complications.

Research motivation

We designed this study to better understand the conduction system disturbances in the setting of severe COVID-19.

Research objectives

To discover the prevalence and types of conduction system disorders in COVID-19 deceased patients as a population representing severe COVID-19.

Research methods

All electrocardiograms of patients who died of COVID-19 in our center were analyzed, and any abnormalities were reported.

Research results

Changes in ST-T were the most common (59%), which indicate myocardial infarction or localized myocarditis. Also, 21.1% showed fragmented QRS and prolonged QTc indicative of myocardial injury. Atrioventricular block (AVB) was found in 9.3% of patients.

Research conclusions

Among patients who expired from COVID-19, ST-T changes are the most common which heralds myocardial damage. Conduction disturbances like AVBs are also important findings and are associated with myocardial damage.

Research perspectives

ECG findings in COVID-19 are variable but mostly involve two pathologies, myocardial damage and conduction system disturbances. Clinicians should be aware of these two complications in the setting of COVID-19 and future research should focus on devising preventive measures to mitigate the cardiovascular complications of COVID-19.

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FOOTNOTES

Author contributions: Nikoo MH contributed to conceptualization, design, data curation, final edit and review, and project administration; Sadeghi A, Estedlal A, and Fereidooni R contributed to writing of the primary draft, final editing and review; Ebrahimi N, Maktabi A, Kamgar M, Mehran F, Mehdibeygi O, Esfandiari H, and Taherinezhad Tayebi M contributed to data collection; Heydari ST contributed to formal analysis and design; all the authors verify the data and are accountable for all aspects of the work.

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