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***Observational Study***

**Conduction system disorders and electrocardiographic findings in COVID-19 deceased patients in 2021, Shiraz, Iran**

Nikoo MH *et al*. Conduction system disorders in COVID-19

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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. This paper can shed light on different conduction disorders seen in COVID-19.

**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 demised 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 ± 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 (± 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 co-morbidities 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 1stdegree 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. 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 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 compilations, 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**

**Institutional review board statement:** This study was reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences (Approval No. IR.SUMS.MED.REC.1400.270).

**Informed consent statement:** The informed consent was waived from the patinets.

**Conflict-of-interest statement:** The authors declare that they have no competing interests.

**Data sharing statement:** Data are available for academic researchers *via* the research deputy of Shiraz Medical School (med\_thesis@sums.ac.ir) upon reasonable request.

**STROBE statement:** The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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**Table 1 Association of patients’ past medical conditions and conduction system disorder in COVID-19 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.

**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** | **Adjusted1 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 |
| S1Q3T3 | 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.



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