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ECG Prediction of Mortality in COVID-19 Patients by Sokolow-Lyon Voltage

Mohammad Hossein Nikoo [1], Alireza Sadeghi [2], Alireza Estedlal [3], Seyyed Taghi Heydari [3,*], Mohammadamir Taherinezhad Tayebi [1], Niloofar Dehdari Ebrahimi [2], Haleh Esfandiari [1], Ali Jamshidi Kerachi [2] and Mahdi Zarourati [2]

[1] Non-communicable Disease Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
[3] Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

[*] *Corresponding author*: Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran. Email: heydari.st@gmail.com

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Abstract

Background: Different electrocardiographic (ECG) results, seen in coronavirus disease 2019 (COVID-19) patients are most likely due to the combined impact of acute COVID-19 and chronic heart disease. Few studies have addressed the effects of hypoxemia, the hallmark of the pandemic disease, on ECG.

Objectives: The present study discusses the prevalence of arrhythmias and disorders of conduction system in demised and survived COVID-19 patients, using ECG and Sokolow-Lyon voltage as a sign of hypoxemia to predict mortality in the admitted patients and after discharge.

Methods: We investigated the ECG, and other medical data of 960 COVID-19 patients admitted to Faghihi hospital in Shiraz, Iran, from August 2021 to December 2021.

Results: Most of the patients were male (541 or 56.4%) and older than 65 years old (462 or 48.1%). A total of 475 (49.5%) patients died. Multiple logistic regression revealed an independent association between the COVID-19 death rate and cardiovascular disease (OR = 3.05; 95% CI: 1.96 - 4.74), QT dispersion more than 40 (OR = 5.08; 95% CI: 3.61 - 7.15), heart rate (more than 100 versus less than 60 OR = 2.86; 95% CI: 1.03 - 7.9), ST segment elevation myocardial infarction (OR = 3.93; 95% CI: 2.63 - 5.86), poor progression (OR = 2.33; 95% CI: 1.56 - 3.49), hypertrophy (OR = 1.97; 95% CI: 1.02 - 3.81), and Sokolow-Lyon (OR = 2.91; 95% CI: 1.64 - 5.16).

Conclusions: Electrocardiographic examination of COVID-19 patients is important during admission and after discharge. Sokolow-Lyon voltage less than 10 can be regarded as an independent predictor of mortality in COVID-19 patients discharged from hospital.

Keywords: COVID-19, Mortality, ECG, Iran

1. Background

Coronavirus disease 2019 (COVID-19) often appears with symptoms and signs of respiratory tract infection, with a relatively high mortality rate (1). Besides, cardiac involvement in respiratory syndromes is usually an ominous sign. COVID-19 adult patients have a wide range of clinical cardiac symptoms. While some patients manifest no clinical evidence of heart disease, some others unveil cardiac manifestations such as myocarditis, myocardial infarction, asymptomatic cardiac arrhythmias, and atrioventricular block (2-4). Nevertheless, owing to mutual symptoms such as dyspnea, chest pain, and cough, diagnosis of cardiac involvement is usually problematic (5, 6).

A variety of cardiac test abnormalities have been demonstrated in COVID-19. Cardiac biomarkers, electrocardiogram, cardiac imaging such as echocardiogram, cardiovascular magnetic resonance, and computed tomography (CT) scan are of great concern to pinpoint the heart involvement. Amongst these tests, electrocardiography (ECG) is simple, widely available, and helpful (6).

Despite the good characteristics of ECG, such as availability, being radiation-free, and non-invasive, the predictive role of ECG in mortality and morbidity of

COVID-19 has not been investigated comprehensively (7-10).

Given that people hospitalized due to COVID-19 have a high prevalence of cardiovascular risk factors, the different ECG readings found in them is most likely due to the combined impact of acute viral sickness and chronic heart disease. The probable mechanisms of these findings include inflammation of myocardium, hyper-aeration insulating effect, positional changes, pulmonary hypertension, and hypoxia itself (11).

Few studies have been conducted on the effects of hypoxemia, the hallmark of the respiratory pandemic disease, in ECG. In 1994, Entwistle et al. used ECG to assess the effect of hypoxemia on the heart at rest (12). Depression of the ST segment during hypoxemia was examined; however, association of this depression with hypoxemia was not established (12). Moreover, Coustet et al. showed that Sokolow-Lyon index decreased by a decrease in arterial oxygen saturation during exercise (13).

2. Objectives

This study aimed to describe the prevalence of ECG abnormalities among deceased and surviving COVID-19 patients and its relationship with mortality.

3. Methods

3.1. Setting and Participants

In this case-control study, a total of 960 COVID-19 patients admitted to the Faghihi hospital in Shiraz, Iran, were enrolled from August 1 to December 1, 2021. The inclusion criteria were age over 18 years; in-patients hospitalized for at least one day; having at least one ECG five days before outcome, at admission, or during admission; and confirmed SARS-CoV-2 by nasopharyngeal sample and polymerase chain reaction (PCR).

Cases and controls were selected using simple random sampling by an independent external researcher among 11,690 participants at Faghihi hospital as the referral center to deliver care to COVID-19 patients in southern Iran. Cases were defined as patients who expired in the course of hospitalization, and controls were unmatched survivors who were discharged and remained alive after one year of hospitalization.

3.2. Variables and Data Collection

We collected the demographic information (age and gender) and ECG variables and patterns of patients. ECG characteristics were defined as rate, atrioventricular blocks (AVB), chamber hypertrophy (HTPh), bundle branch blocks (BBB), poor R wave progression, ventricular infarction, QT dispersion, and Soklow-Lyon voltage. Those who did not have ECG were excluded from the survey.

All the ECGs were taken by multiple independent trained technicians using 12-lead electrocardiography devices. All the technicians were blinded to the patients' medical conditions. Two independent cardiologists interpreted each ECG under the supervision of a cardiac electrophysiologist. All these people were blinded to the patients' demographics, medical history, and outcomes. Sokolow-Lyon voltage was defined as the height of R wave in V5 V6 (the taller one) plus depth of S wave in V1 or V2 (the deepest one). The QT dispersion was defined as the longest QT in any lead from the shortest one in any other lead. Also, the treatment method was the standard protocol for COVID-19 at that time, which was not different between the survived and expired patients.

3.3. Data Analysis

The statistical package for the social sciences version 21.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the collected data. frequency (%) was used for categorical variables such as sex, alcohol dependency, and ECG findings. Odds ratio (OR) and confidence interval (95% CI) were utilized to investigate the correlation between COVID-19 mortality and ECG variables (AVB, HTPh, BBB, poor R wave progression, ventricular infarction, QT dispersion, and Soklow-Lyon voltage), age category, sex, comorbidity diseases, and smoking. The independent correlation between COVID-19 mortality and ECG variables was determined using multiple logistic regression adjusted for sex and age. P-value less than 0.05 was considered as statistically significant.

4. Results

Among the 960 patients, 541 (56.4%) were male, and 475 (49.5%) were expired. The mean age of participants was 62.36 ± 15.66 years. The most prevalent comorbidities were hypertension (42.0%), diabetes mellitus (32.6%), heart diseases (20.5%), coronary disease (18.5%), hyperlipidemia (12.2%), lung disease (5.1%), and chronic kidney disease (4.5%). The cause of mortality was respiratory failure unresponsive to mechanical ventilation, and arrhythmic death was less than one percent. Also, the most frequent arrhythmias were AF (2.5%) and PVC (1.2%).

4.1. Univariate Analysis

In the univariate analysis, sex (male OR = 1.35; 95% CI: 1.05 - 1.75), age range of above 40 years old (age 50 - 65 years old OR = 2.19; 95% CI: 1.48 - 3.24, age more than 65

years old OR = 3.7; 95% CI: 2.57 - 5.34), chronic kidney disease (OR = 1.99; 95% CI: 1.05 - 3.78), hypertension (OR = 1.46; 95% CI:1.13 - 1.89), heart disease (OR=5.04; 95% CI: 3.49 - 7.28), QT dispersion more than 40 (OR = 9.82 ; 95% CI: 7.05 - 13.69), atrioventricular conduction block (OR = 4.06; 95% CI: 2.19 - 7.52), heart rate (more than 100 versus less than 60 OR = 2.63; 95% CI: 1.12 - 6.18), ST segment elevation myocardial infarction (OR=5.85; 95% CI: 4.22 - 8.1), bundle branch block (OR=5.03; 95% CI: 3.64 - 6.9), poor progression (OR = 2.22; 95% CI:1.56 - 3.18), hypertrophy (OR = 2.57; 95% CI: 1.56 - 4.24), and Sokolow-Lyon (OR = 3.1; 95% CI: 2.01 - 4.78) were significantly associated with COVID-19 mortality rate (Table 1).

4.2. Multiple Analysis

In multiple logistic regression, there was an independent relationship between COVID-19 mortality rate with sex (male OR = 1.51; 95% CI: 1.08 - 2.1), age range of above 40 years old (age 50 - 65 years old OR = 2.45; 95% CI: 1.51 - 3.99), age more than 65 years old (OR = 2.73; 95% CI: 1.73 - 4.31), heart disease (OR = 3.05; 95% CI: 1.96 - 4.74), QT dispersion more than 40 (OR = 7.51; 95% CI: 5.2 - 10.84), heart rate (more than 100 versus less than 60 OR = 2.87; 95% CI: 1.05 - 7.87), ST segment elevation myocardial infarction (OR = 4.35; 95% CI: 2.93 - 6.45), poor progression (OR = 2.87; 95% CI: 1.93 - 4.25), hypertrophy (OR = 2.02; 95% CI: 1.07 - 3.81), and Sokolow-Lyon (OR = 2.55; 95% CI: 1.47 - 4.41) (Table 1).

5. Discussion

This study aimed to find the predictors of mortality from ECG. In order of significance, the evaluated electrocardiographic parameters were QT dispersion (14), myocardial infarction (15), Sokolow-Lyon voltage, poor R wave progression (16), and hypertrophy (17). The single most conspicuous observation to emerge from the data comparison was that the only remaining predictor of death after discharge was Sokolow-Lyon voltage.

Mortality rate was higher among males than females, which is in line with previous reports (18). In addition, older age increased COVID-19 mortality, as mentioned by Clara Bonanad in a recent meta-analysis (19).

In our study, there was a significant rise in mortality due to signs of cardiac involvement in COVID-19, which is consistent with some previous results. This risk was mainly observed by four times for myocardial infarction, 2.59 times for poor R progression, and of 1.6 times for atrioventricular block (15, 16, 20-22). Besides, hypertrophy, either as an indicator of previously diseased heart or a heart facing an acute pressure overload, also increased the risk more than two times (17).

QT dispersion more than 40 milliseconds was five times more prevalent in demised patients (14). This QT dispersion is known as an indirect predictor of sudden cardiac death because of repolarization inhomogeneity. This can be due to copious number of inflammatory mediators and their effect on myocardium (23).

We also witnessed a reduction in the Sokolow-Lyon voltage in demised patients. Sokolow-Lyon voltage is used most frequently in cardiology to diagnose left ventricular hypertrophy (24-26). This voltage was reported to be smaller in hypoxemia by Baptiste Coustet et al. (13). The decline in voltage during hospitalization, especially when the disease progressed to a critical stage, could indicate COVID-19-related heart and lung damage (8). This supports previous findings by Gupta et al. that reported a decrease in QRS voltage in COVID-19 patients (27).

Accordingly, in this study, Sokolow-Lyon below 10 was compared between demised and survived patients. The odds ratio was nearly 3.5 in univariate analysis and 2.55 when adjusted for age, sex, and ECG. The predictive value of the voltage in the mortality of COVID-19 patients can be explained by several hypotheses. First, the hypoxic effect of COVID-19 can decrease the electrical power of left ventricle (13). Second, it has been known that pulmonary diseases - similar to what happens in emphysematous patients - can result in the hyper-aeration and reduction in electrical conduction (11, 27). Finally, right ventricular hypertrophy or dilatation confronts the left voltage and causes its reduction (24, 28).

Furthermore, the reduction in Sokolow-Lyon voltage was also assessed in patients after discharge from hospital. We observed a significant association between the Sokolow-Lyon voltage below 10 and mortality with the odds ratio of 3.57 in the demised patients after discharge. This new observation may be a sign of continued hypoxia effects and complication on myocardium despite recovered lung function (29).

5.1. Conclusions

Electrocardiographic examination of COVID-19 patients is important during admission and after discharge. In COVID-19 patients discharged from hospital, Sokolow-Lyon voltage less than 10 can be regarded as an independent predictor of mortality.

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Table 1. Association Between Death and ECG Variables in COVID-19 Mortality with Univariate and Multiple Logistic Regressions

Variables	Status		Odds Ratio (95% CI) Univariate	P Value	Odds Ratio (95% CI) Multiple [a]	P Value
	Survived	Expired				
Sex						
Female	248 (59.19)	171 (40.81)	1	-	1	-
Male	280 (51.76)	261 (48.24)	1.35 (1.05 - 1.75)	0.022	1.35 (0.97 -1.89)	0.080
Age						
< 50	152 (74.88)	51 (25.12)	1	-	1	-
50 - 64	170 (57.63)	125 (42.37)	2.19 (1.48 - 3.24)	< 0.001	1.51 (0.95 - 2.39)	0.080
≥ 65	206 (44.59)	256 (55.41)	3.7 (2.57 - 5.34)	< 0.001	1.42 (0.9-2.24)	0.132
QT dispersion						
< 40	311 (84.97)	55 (15.03)	1	-	1	-
≥ 40	217 (36.53)	377 (63.47)	9.82 (7.05 - 13.69)	< 0.001	5.08 (3.61 - 7.15)	< 0.001
AVB						
No	514 (56.92)	389 (43.08)	1	-	1	-
Yes	14 (24.56)	43 (75.44)	4.06 (2.19 - 7.52)	< 0.001	1.56 (0.74 - 3.3)	0.245
Heart rate						
60 - 100	18 (66.67)	9 (33.33)	1	-	1	-
< 59	434 (57.33)	323 (42.67)	1.49 (0.66 - 3.36)	0.338	1.76 (0.67 - 4.61)	0.252
> 100	76 (43.18)	100 (56.82)	2.63 (1.12 - 6.18)	0.026	2.86 (1.03 - 7.9)	0.043
STEMI						
No	466 (65.73)	243 (34.27)	1	-	1	-
Yes	62 (24.7)	189 (75.3)	5.85 (4.22 - 8.1)	< 0.001	3.93 (2.63 - 5.86)	< 0.001
BBB						
No	470 (58.1)	339 (41.9)	1	-	1	-
Yes	58 (38.41)	93 (61.59)	5.03 (3.64 - 6.96)	< 0.001	1.08 (0.67 - 1.74)	0.751
Poor progression						
No	464 (64.53)	255 (35.47)	1	-	1	-
Yes	64 (26.56)	177 (73.44)	2.22 (1.56 - 3.18)	< 0.001	2.33 (1.56 - 3.49)	< 0.001
Hypertrophy						
No	503 (56.77)	383 (43.23)	1	-	(-)	
Yes	25 (33.78)	49 (66.22)	2.57 (1.56 - 4.24)	< 0.001	1.97 (1.02-3.81)	0.044
Sokolow-Lyon						
≤ 10	495 (58.03)	358 (41.97)	1		1	-
> 11	33 (30.84)	74 (69.16)	3.1 (2.01 - 4.78)	< 0.001	2.91 (1.64 - 5.16)	< 0.001
Chronic kidney disease						
No	470 (51.65)	440 (48.35)	1	-	1	-
Yes	15 (34.88)	28 (65.12)	1.99 (1.05 - 3.78)	0.035	1.55 (0.69 - 3.48)	0.288
Diabetes						
No	338 (52.81)	302 (47.19)	1	-	1	-
Yes	147 (46.96)	166 (53.04)	1.26 (0.96 - 1.66)	0.090	0.97 (0.67 - 1.4)	0.854
Hypertension						
No	303 (54.89)	249 (45.11)	1	-	1	-
Yes	182 (45.5)	218 (54.5)	1.46 (1.13 - 1.89)	0.004	1.10 (0.76 - 1.58)	0.625
Cerebrovascular accident						
No	468 (51.6)	439 (48.4)	1	-	1	-
Yes	17 (38.64)	27 (61.36)	1.69 (0.91 - 3.15)	0.096	1.21 (0.55 - 2.66)	0.631
Hyperlipidemia						
No	424 (50.72)	412 (49.28)	1	-	1	-
Yes	61 (52.14)	56 (47.86)	0.95 (0.64 - 1.39)	0.774	0.79 (0.47 - 1.32)	0.363
Autoimmune						
No	462 (51.22)	440 (48.78)	1	-	1	-
Yes	23 (45.1)	28 (54.9)	1.28 (0.73 - 2.25)	0.396	1.65 (0.81 - 3.36)	0.168
Heart disease						
No	442 (58.47)	314 (41.53)	1	-	1	-
Yes	43 (21.83)	154 (78.17)	5.04 (3.49-7.28)	< 0.001	3.05 (1.96 - 4.74)	< 0.001
Smoking						
No	454 (52.24)	415 (47.76)	1	-	1	-
Yes	31 (36.9)	53 (63.1)	1.87 (1.18 - 2.97)	0.008	1.17 (0.64 - 2.12)	0.617

Abbreviations: AVB, atrioventricular conduction block; STEMI, segment elevation myocardial infarction; BBB, bundle branch block.
[a] P-value less than 0.05 was considered significant.

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Footnotes

Authors' Contribution: MHN, STH, AS, and MTT analyzed data, interpreted the results, and wrote the manuscript draft. MHN and STH interpreted the results and designed the study. AE, NDE, HE, AJK, and MZ interpreted the results and wrote the manuscript draft. All authors have read and approved the manuscript.

Conflict of Interests: One of the authors (STH) of this study is a member of the editorial board. The journal confirmed that the mentioned author with CoI was completely excluded from all review processes. We also introduced this author with CoI during the submission as an opposed reviewer.

Ethical Approval: This study was approved by the ethical board of Shiraz University of Medical Sciences (code: IR.SUMS.REC.1400.270).

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