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Original article

Electrocardiographic Predictors of Adverse Outcomes Among Hospitalized COVID-19 Patients

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Abstract

Background: There is growing evidence of cardiac injury in COVID-19. Minor studies examine electrocardiographic alterations at admission and during hospitalization are associated with major events and infection severity. Some reports that specific experimental therapies might cause QTc prolongation in COVID-19 patients may predispose them to arrhythmic complications. ***Objectives:*** to evaluate the relationship between electrocardiogram parameters and clinical outcomes of death, duration of hospitalization, and mechanical ventilation among patients hospitalized due to COVID-19 infection. ***Methods:*** The study included all verified COVID-19 patients hospitalized in a dedicated ward between March 2020 and March 2021. Inclusion criteria were the availability of admission-electrocardiogram and sufficient clinical data. In-hospital mortality, duration of hospitalization, and mechanical ventilation were defined as dependent indicators of major adverse events. ECGs were imported using a high-resolution scanner, and intervals were measured in a blinded manner using an on-screen digital calliper. The ECG parameters were computed with a designated algorithm from the bipolar and unipolar limb leads. Average RR interval, a standard deviation of normal-to-normal R-R intervals (SDNN), root mean square of successive differences between normal heartbeats (RMSSD), average QT, QT-peak, Tpeak-end, QTc, Tp-end/QT, and QRS durations were computed. Bivariate regression analyses between ECG parameters and clinical data were estimated with the Pearson correlation coefficient (r). ***Results:*** The cohort included 280 patients, of whom 100 had ECG results. Twenty included patients died in the hospital. Significant positive correlations were found between mortality and mean QRS. None of the other parameters reached statistical significance. ***Conclusions:*** High admission values of ECG-derived 10-sec QRS durations are associated with a high mortality rate in COVID-19 patients. Further prospective large-scale trials should be performed to corroborate these results and determine the role of other clinical modifiers.

Keywords: ***COVID-19, Electrocardiographic, In-hospital Mortality, Duration of hospitalization, Mechanical ventilation.***

Introduction

Coronavirus Disease 2019 (COVID-19) is caused by the novel Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). In February 2020, the World Health Organization designated COVID-19 as a clinical condition caused by a virus identified as a cluster cause of pneumonia in Wuhan, China [1]. Shortly after that, the virus spread worldwide, wreaking havoc on the medical system and paralyzing the global economy.

Several risk factors have been associated with COVID-19 severity and outcomes. Several cardiovascular complications have been reported, such as acute coronary syndrome, myocarditis, takotsubo cardiomyopathy, right ventricular dysfunction, and cor pulmonale [2-7]. These are common and confer worse outcomes among patients admitted with COVID-19. At the beginning of the pandemic, there were concerns that specific experimental therapies like antimalarials (hydroxychloroquine) might cause QTc prolongation in COVID-19 patients and predispose them to arrhythmic complications.

There are several pathophysiologic pathways of cardiac involvement related to COVID-19, including cytokine storm and hypoxia, which induce excessive intracellular calcium leading to cardiac myocyte apoptosis; myocardial ischemia from epicardial and microvascular coronary thrombosis caused by the hypercoagulable state associated with COVID-19; demand-supply mismatching from hypoxemia and shock; systemic inflammation, and direct viral myocardial infiltration leading to myocarditis [8-12]. The exact mechanism of cardiac involvement remains unclear.

A clinical tool like troponin and electrocardiogram can reveal a broad spectrum of cardiovascular complications. Timothy et al. [13] concluded that myocardial injury with hs-cTnT ≥ 20 ng/L and cardiac arrhythmia, especially atrial fibrillation/flutter among patients hospitalized with COVID-19 infection, is associated with a marked increase in the risk for mortality. A trial describing electrocardiogram features of patients with COVID-19 pneumonia during hospitalization is underway [14]. However, whether specific electrocardiographic predictors recorded on admission can be used to identify patients who are more likely to develop adverse outcomes is unknown.

This study aimed to investigate the relation between electrocardiogram parameters and major adverse events, considered as the composite of all-cause in-hospital mortality, duration of hospitalization, and mechanical ventilation, to define their predictive value.

Methods

This retrospective cohort study included all verified COVID-19 patients hospitalized from March 2020 through March 2021 in a tertiary care medical center. Inclusion criteria were the availability of admission-electrocardiogram and sufficient clinical data. In-hospital mortality, duration of hospitalization, and mechanical ventilation were defined as dependent indicators of major adverse events. ECGs were imported using a high-resolution scanner, and intervals were measured in a blinded manner using an on-screen digital calliper by one researcher and checked by another. Average RR interval, a standard deviation of normal-to-normal R-R intervals (SDNN), root mean square of successive differences between normal heartbeats (RMSSD), average QT, QT-peak, Tpeak-end, QTc, Tp-end/QT, and QRS durations were computed using a designated algorithm from the bipolar and unipolar limb leads. Exclusion criteria include preexisting bundle branch blocks or Pacemaker rhythm, cardiac arrhythmias, and antiarrhythmic medications.

Bivariate regression analyses between ECG parameters and clinical data were calculated with the Pearson correlation coefficient (r).

Results

The cohort included 280 COVID-19 patients hospitalized from March 2020 through March 2021. Among them, 100 had ECG performed on admission. Twenty of the 100 patients died during hospitalization and were on mechanical ventilation. Significant positive correlations were found between mortality and mean QRS (**Figure 1, Table 1**). Table 2 shows a positive correlation between mean QT-peak and hospitalization but does not reach statistical significance. In Table 3, there are positive correlations but not substantial statistically between mean QRS and QTc to mechanical ventilation. None of the other parameters reached statistical significance.

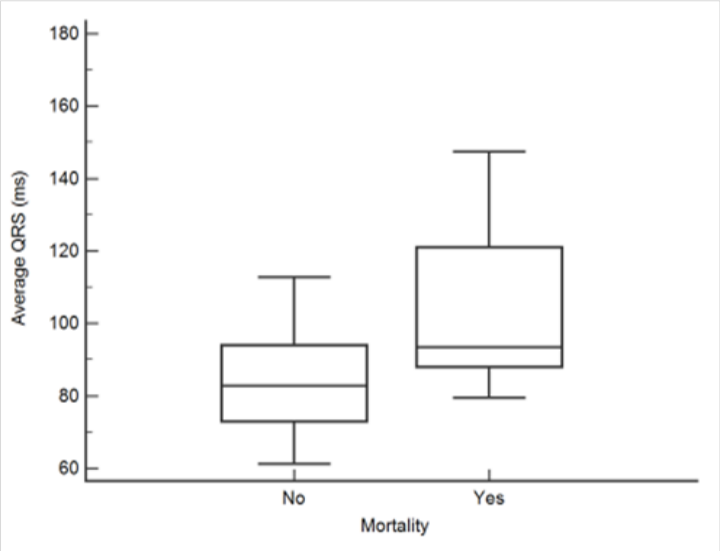

Figure 1: Correlation between average QRS and mortality over COVID patients.

Table 1: Correlation analysis between ECG parameters on admission with COVID patients survivors and non-survivors.

ECG parameters	COVID 19 survivors (n=80)	COVID 19 related Mortality (Yes, n=20)	P value**
Mean RR (ms)	**787.8± 28.2***	**763.7±42.6**	0.84
SDNN (ms)	18.3± 5.9	33.7± 15.4	0.65
RMSSD (ms)	26.5± 9.5	45.3± 22.7	0.92
Mean QT (ms)	371.1± 9	374.8± 13.4	0.55
Mean QT-peak(ms)	284.04± 7.3	289.4± 12	0.49
Mean T peak-end(ms)	86.3± 4.1	82.7± 6.9	0.69
Mean QRS (ms)	90.7± 4	103.8± 6.9	0.03
QTc(ms)	423.5± 7	429.9± 11.9	0.31
Mean T peak-end/QT (ms)	0.7	0.7±0.01	0.63

** Results by means ± Std Err Mean*

*** P-value<0.05 statistical significance.*

Table 2: Correlation between ECG parameters on admission and hospitalization

ECG parameters	Hospitalization (n=100) *	
	R**	P-value***
Mean RR	0.146	0.30
SDNN	0.131	0.35
RMSSD	0.145	0.30
Mean QT	0.212	0.13
Mean QT-peak	0.239	0.09
Mean T peak-end	0.093	0.52
Mean QRS	0.075	0.6
QTc	0.170	0.23
Mean T peak-end/QT	0.092	0.51

* Numbers of COVID patients included in the study.

**Correlation coefficient r.

*** P-value<0.05 statistical significance.

Table 3: Correlation analysis between ECG parameters on admission and need for respiratory support

ECG parameters	Non-invasive respiratory support (n=80)	Mechanical ventilation (n=20)	P-value*
Mean RR (ms)	778.25± 26.94*	803.04± 55.8	0.68
SDNN (ms)	22.373± 6.81	17.34± 7	0.77
RMSSD (ms)	31.2± 10.65	26.19± 12	0.53
Mean QT (ms)	365.77± 7.26	396.95±25.01	0.25
Mean QT-peak(ms)	280.43± 6.35	304.30±18.31	0.26
Mean T peak-end(ms)	83.67± 3.95	94.63±9.28	0.21
Mean QRS (ms)	91.11± 3.69	102.31±10.15	0.13
QTc(ms)	420.56± 6.63	442.45±15.20	0.09
Mean T peak-end/QT (ms)	0.766±0.007	0.768±0.014	0.94

** P-value<0.05 statistical significance.*

Discussion

This study evaluated ECG parameters at admission to predict prognosis among patients hospitalized with SARS-CoV-2. We found that ECG at admission is useful for identifying patients with poorer in-hospital clinical outcomes. The ECG findings at admission could be a marker to identify subgroups of patients with COVID-19 at greater risk for adverse clinical outcomes. Therefore, ECG at admission could help clinicians stratify the overall risk in COVID-19 patients.

ECG is a valuable tool in everyday practice to recognize myocardial damage due to its widespread availability. Interestingly, abnormal changes seen on 12-lead electrocardiograms were directly associated with in-hospital mortality of COVID-19 patients.

A recent study [15] checked ECG parameters at admission and after seven days of hospitalization. Abnormal ECG at admission and elevated baseline troponin I values were more common among patients who developed major adverse events. In addition, primary ST-T changes and signs of left ventricle hypertrophy were associated with a worse prognosis. Also, abnormal ECG on seven days was related to a major adverse event.

Another Italian study [16] found that ECG abnormalities at admission were common in COVID-19 infection and related to higher mortality risk. On the other hand, sinus rhythm at admission has been associated with lower mortality.

A large trial [17] manifested that the combination of abnormal respiratory vital signs and ECG findings of atrial fibrillation/flutter, right ventricular strain or ST-segment abnormalities accurately prognosticated early deterioration in patients with COVID-19. We found that widened QRS increased in-hospital mortality, and increased QTc caused more need for invasive ventilation.

This study had some limitations. First, it was done in a single medical center, and the small number of patients limited the statistical power of the analyses. Due to various logistical issues, ECGs were not performed for hospitalized patients, which explains why we use only ECG parameters at admission. Also, echocardiography was not routinely performed in these patients.

Conclusion

High values of ECG-derived 10-sec QRS durations at hospital admission were associated with high mortality rates in COVID-19 patients. Prospective, large-scale trials are needed to corroborate these results and determine the role of other clinical cardiac modifiers in predicting mortality from COVID-19.

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Non

Conflict of interest

The authors declare no potential conflict of interest.

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