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The prognostic significance of electrocardiography findings in patients with coronavirus disease 2019: A retrospective study at tertiary care hospital from north India

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Abstract

There is growing evidence of cardiac injury in COVID-19. Our purpose was to assess the prognostic value of serial electrocardiograms in COVID-19 patients. Coronavirus disease 2019 (COVID-19) has reached a pandemic level. Cardiac injury is not uncommon among COVID-19 patients. We attempted to describe the electrocardiographic characteristics and to identify the prognostic significance of electrocardiography (ECG) findings of patients with COVID-19.Consecutive patients with laboratory-confirmed COVID-19 and definite in-hospital outcome were retrospectively included. Demographic characteristics and clinical data were extracted from medical record. Initial ECGs at admission and thereafter during hospitalization were reviewed. A point-based scoring system of abnormal ECG findings was formed, in which 1 point each was assigned for the presence of axis deviation, arrhythmias, atrioventricular block, conduction tissue disease, QTc interval prolongation, pathological Q wave, ST-segment change, and T-wave changes. The association between abnormal ECG scores and in-hospital mortality was assessed in multivariable Cox regression models.

Total of 612 patients were included. T-wave change (31.7%), QTc interval prolongation (30.1%), and arrhythmias (16.3%) were three most common found ECG abnormalities. 60 (9.80%) patients died during hospitalization. Abnormal ECG scores were significantly higher among non-survivors (median 2 points vs 1 point, $p < 0.001$). The risk of in-hospital death increased by a factor of 1.478 (HR 1.478, 95% CI 1.131–1.933, $p = 0.004$) after adjusted by age, comorbidities, cardiac injury and treatment. ECG abnormality was associated with higher risk of death.ECG abnormality was common in patients admitted for COVID-19 and was associated with adverse in-hospital outcome. In-hospital mortality risk increased with increasing abnormal ECG scores.

Keywords: prognostic, electrocardiography, coronavirus disease, retrospective

Introduction

Since December 2019, coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quickly spread throughout the world and caused a global pandemic [1, 2, 3, 5, 9] Although clinical manifestations of COVID-19 were mainly respiratory, cardiac injury, and arrhythmias were not uncommon and the association between cardiac injury and poor in-hospital outcome had been determined[3,4,5] As a simple and easily obtainable tool to identify patients with acute or chronic cardiac disease, ECG is frequently performed in patients with cardiovascular disease and was also studied in pneumonia [6, 7, 8, 9], severe acute respiratory syndrome (SARS) [10, 11, 12, 13] and Middle East respiratory syndrome (MERS) [14, 15, 16] However, systematic studies of ECG characteristics in COVID-19 patients were limited [7, 8] and its prognostic significance remained to be fully elucidated [17, 18, 19]. The purpose of this study was to describe the electrocardiographic characteristics and to identify the prognostic significance of ECG findings at admission or during hospitalization in patients with COVID-19 [20, 21]. Coronavirus disease 2019 (COVID-19) is a global pandemic, as World Health Organization (WHO) declared on March 11, 2020. COVID-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2): this single-stranded enveloped RNA virus interacts through binding of surface spike protein human angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is expressed in the lung and intestinal epithelium, vascular endothelium, kidneys, and heart as well (Tikellis & Thomas, 2012) [20]. The exact mechanism of cardiac involvement remains unclear. Probably, it is not only related to the interaction between protein and receptor. Other suggested mechanisms of COVID-19 related to cardiac involvement include cytokine storm and hypoxia inducing excessive intracellular calcium leading to cardiac myocyte apoptosis (Zheng *et al*., 2020) [24]. Myocardial injury was found among early cases in China. Previous studies had confirmed that cardiac injury (elevated high-sensitivity Troponin I or new ECG or echocardiographic abnormalities) was present in 7 to 1% of patients overall, and 26% required intensive care (Wang *et al*., 2020) [4]. A recent study of Shi *et al*. comparing 82 COVID-19 patients with and without cardiac injury concluded that cardiac injury is associated with a high risk of in-hospital mortality ECG changes during viral infections were previously studied: ECG abnormalities during the 2009 H1N1 influenza infection were transient and not correlated with preexisting patient characteristics or with outcomes (Akritidis *et al*., 2010) [9].

No specific ECG changes have been described in patients with SARS-CoV2 infection yet. The real prevalence of ECG anomalies and the incidence of benign and malignant arrhythmias in COVID-19 infection is still not well defined (Kochi *et al*., 2020) [13].

This study aims to investigate the relationship between abnormal serial ECG findings in patients with COVID-19

and major adverse events (MAE), considered as the composite of all-cause intra-hospital mortality or respiratory failure requiring orotracheal intubation (OTI), to define their prognostic value.

Method

We evaluated 612 consecutive patients admitted to our center with confirmed SARS-CoV-2 infection. ECGs available at admission and thereafter during hospitalization were assessed. We evaluated the correlation between ECGs findings and major adverse events (MAE) as the composite of intra-hospital all-cause mortality or need for invasive mechanical ventilation. Abnormal ECGs were defined if primary ST-T segment alterations, left ventricular hypertrophy, tachy or bradyarrhythmias and any new AV, bundle blocks or significant morphology alterations (e.g., new Q pathological waves) were present

In this single center, observational study, consecutive patients with laboratory SARS-Cov-2 RNA detection confirmed COVID-19 and definite in-hospital outcome admitted in Era Lucknow Medical College & Hospital, Lucknow, India from March 2020 to June 2021 were retrospectively included. Throat and nasal-swab specimens were obtained for SARS-CoV-2 detection from suspected patients using real-time polymerase chain reaction (PCR) assay, which was performed in our hospital at Lucknow, India.

Clinical data collection

Demographic information (age and sex) and clinical data consisting of disease duration, blood pressure at admission, comorbidities, serum level of high-sensitive cardiac troponin I (hs-cTnI), and treatment data were extracted from medical record. Disease duration was defined as time from symptom onset to admission. Cardiac injury was diagnosed if serum level of hs-cTnI was above the 99th percentile upper reference limit (which was 0.026ug/L in our hospital).

12-Lead electrocardiography

Resting standard 12-lead ECGs were performed in all patients at admission or during hospitalization using a paper speed of 25 mm/s and a sensitivity of 1 mV = 10 mm. The initial ECG record of each patient was reviewed. Heart rate, PR interval, QTc interval (corrected by Bazett's formula) and mean frontal plane QRS electrical axis were measured automatically by the ECG machine/computer-generated measurements. ECG parameters (definitions listed in the Table-1) were reviewed and confirmed by investigators.

Patients were considered to have arrhythmias if they had sinus tachycardia, sinus bradycardia, sinus node arrest or atrial fibrillation and were considered to have conduction tissue disease if they had right bundle branch block (RBBB), left bundle branch block (LBBB), or left anterior fascicular block(LAFB) [10] ST-segment change included ST-elevation and ST-depression and T-wave change was consisted of inverted T-wave and flat T-wave To evaluate the prognostic significance of abnormal ECG findings, we created a point-based scoring system, in which 1 point each was assigned for the presence of axis deviation arrhythmias, atrioventricular block, conduction tissue disease, QTc interval prolongation, pathological Q wave, ST-segment change and T-wave change. We calculated abnormal ECG scores by adding 1 point each for any of the eight ECG findings aforementioned. Such ECG scoring was analyzed as a continuous variable.

In-hospital outcome

All patients were followed up during hospitalization. The in-hospital outcome comprised incidence of in-hospital death or discharge. Patients were discharged if they had relieved clinical symptoms, normal body temperature, significant resolution of inflammation as shown by chest radiography and negative results shown by real-time PCR assay for COVID-19 [11] The vital status of patients was determined by medical record. Discharged patients were censored on the date of discharge.

Statistical analysis

Continuous variables are presented as means with standard deviations (SD) for normally distributed data or median with interquartile range (IQR) for non-normal distribution. Normal distribution of variables was assessed by the Kolmogorov–Smirnov test. Categorical variables were expressed as frequencies and percentages. Patients were categorized as non-survivors versus survivors. Student's *t* test or the Mann–Whitney test was used to test intergroup differences in continuous variables where appropriate. Differences in categorical variables were tested by Fishers' exact test. Univariable and multivariable Cox regression were used to analyze the association between baseline variables and in-hospital death. Variables that were significantly associated with in-hospital death ($p < 0.05$) in the univariable analysis were retained in the multivariable model

To evaluate the association between abnormal ECG and in-hospital death, we established two Cox regression models. In model 1, univariable and multivariable Cox regression were firstly performed on variables including age, comorbidities, cardiac injury and abnormal ECG. Secondly, variables consisting of treatment with glucocorticoid, antiviral and mechanical ventilation were added to the identified independent variables in model 1 to assess whether they maintained a significant association with in-hospital mortality (model 2). The statistical analysis was performed in SPSS (version 19.0). *p*-values <0.05 (2-sided) were considered statistically significant.

Result

Patient Characteristic

A total of 612 patients with laboratory confirmed COVID-19 were admitted in our hospital from March 2020 to June 2021 and included in the present study. The mean age of this cohort was 62.84 ± 14.69 years old A total of 314 patients (51.3%) were with comorbidities. The proportion of hypertension, diabetes, coronary artery disease, previous stroke, atrial fibrillation history, chronic kidney disease, and chronic obstructive pulmonary disease was 41.8% (256 patients), 16.7% (102 patients), 12.1% (74 patients), 7.8% (48 patients), 0.7% (4 patients), 5.2% (32patients), and 3.9% (24 patients), respectively. The proportion of cardiac injury was 14.4% (88 patients) and the median serum level of hs-cTnI was 0.005 (range 0.000–4.700, IQR 0.001,0.012) μg/L. Compared with survivors, non-survivors were older (mean age 79.17 ± 8.80 vs 61.07 ± 14.10, $p < 0.001$) and had a higher proportion of comorbidities (83.3% vs 47.8%, $p < 0.001$) and more likely to have cardiac injury (70.0% vs 8.3%, $p < 0.001$). The median serum hs-cTnI level was also higher among non-survivor group (0.048 [0.023,0.174] vs

0.004 [0.001,0.009] μg/L, $p < 0.001$). Non-survivors had significantly faster heart rate. The proportion of sex, disease duration and blood pressure at admission of the two groups were similar. Baseline demographic and clinical characteristics were listed in Table-1

Table 1: Comparison of demographics, clinical characteristics and treatments between non-survivors versus survivors

Variables	All patients (*n* = 612)	Non-survivors (*n* = 60)	Survivors (*n* = 552)	*p*-value
Demographics characteristics				
Male – *n* (%)	294 (48%)	38 (63%)	256 (46%)	0.086
Female	318(52%)	22(37%)	296(54%)	0.088
Age, years	63 ± 15	79 ± 9	61 ± 14	<0.001
Clinical characteristics				
Disease duration, days	7 (5–12)	8(5–10)	7(5–12)	0.799
Heart rate	80 (70–93)	95 (83–106)	78 (70–91)	<0.001
SBP on admission, mmHg	130 (120–140)	131 (120–144)	130 (120–140)	0.674
DBP on admission, mmHg	79 (71–85)	80 (69–87)	79 (71–85)	0.854
Comorbidities – *n* (%)	314 (51%)	50 (83%)	264 (48%)	<0.001
Hypertension – *n* (%)	256(42%)	42 (70%)	214 (39%)	0.001
Diabetes – *n* (%)	102 (17%)	16(27%)	86 (16%)	0.126
CAD – *n* (%)	74 (12%)	20 (33%)	54 (10%)	0.001
Previous stroke – *n* (%)	48(8%)	16(27%)	32(6%)	0.001
AF history – *n* (%)	4 (0.7%)	2(3%)	2 (0.4%)	0.187
CKD – *n* (%)	32 (5%)	14 (23%)	18(3%)	0.001
COPD – *n* (%)	24 (4%)	10(17%)	14(3%)	0.003
hs-cTnI (μg/L)	0.005 (0.001–0.012)	0.048 (0.023–0.174)	0.004 (0.001–0.009)	<0.001
Cardiac injury – *n* (%)	88 (14%)	42 (70%)	46 (8%)	<0.001
Hospital stay, days	44(13–29)	24(6–18)	46 (14–30)	<0.001
Treatment				
Antivirus – *n* (%)	602 (98%)	58 (97%)	544 (99%)	0.405
Glucocorticoid – *n* (%)	204 (33%)	54 (90%)	150 (27%)	<0.001
Mechanical ventilation – *n* (%)	100(16.33%)	60 (9.8%)	40 (6.5%)	<0.001

- *Note*: Statistically significant *p*-values ($p < 0.05$) are shown in bold.
- Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; hs-cTnI, high-sensitive cardiac troponin I; SBP, systolic blood pressure.

Overall, majority of patients were treated with antivirus (602 patients, 98.4%). The proportion of Favipiravir and remdesivir was 90.8% (556 patients) and 16.3% (100 patients) respectively. The proportion of patients treated with glucocorticoid was 33.3% (204 patients). Mechanical ventilation was used in 100 patients (16.33%). Compared with survivors, non-survivors presented with a significantly higher proportion of glucocorticoid (90.0% vs 27.2%, $p < 0.001$) and mechanical ventilation therapy (20.0% vs 0.4%, $p < 0.001$). Treatment data are depicted in Table-1

ECG findings

Initial ECGs were performed at admission (within 48 h) in 548 (89.5%) patients. The remaining 64(10.5%) patients underwent ECGs examination during hospitalization with median 14 (8.3,18.0) days after admission. As shown in Table-1, T-wave change (194 patients, 31.7%) was the most common abnormal finding and QTc interval prolongation, arrhythmias, axis deviation, conduction tissue disease, ST-segment change, atrioventricular block and pathological Q wave were present in 184 patients (30.1%), 100 patients (16.3%), 68 patients (11.1%), 56 patients (9.2%), 48 patients (7.8%), 24 patients (3.9%), and 12 patients (2.0%), respectively.

Table 2: Comparison of ECG findings between non-survivors versus survivors

Variables	All patients (*n* = 612)	Non-survivors (*n* = 60)	Survivors (*n* = 552)	*p*-value
Axis deviation – *n* (%)	68 (11%)	20 (33%)	48 (9%)	<0.001
Right-axis deviation-*n* (%)	14 (2%)	6 (10%)	8 (1%)	0.023
Left-axis deviation –*n* (%)	52 (9%)	12 (20%)	40 (7%)	0.030
Extremely axis deviation – *n* (%)	2 (0.3%)	2 (3%)	0 (0%)	0.098
Arrhythmias – *n* (%)	100 (16%)	24 (40%)	76 (14%)	0.001
Sinus tachycardia –*n* (%)	58 (10%)	14 (23%)	44 (8%)	0.014
Sinus bradycardia –*n* (%)	20 (3%)	0 (0%)	20 (4%)	0.606
Sinus node arrest –*n* (%)	2 (0.3%)	2 (3%)	0 (0%)	0.098
AF –*n* (%)	20 (3%)	8 (13%)	12(2%)	0.010
AVB – *n* (%)	24 (4%)	6 (10%)	18 (3%)	0.102
First degree AVB – *n* (%)	20 (3%)	4 (7%)	16 (3%)	0.256
Second degree AVB Mobitz type I – *n* (%)	4 (0.7%)	2 (3%)	2 (0.4%)	0.187
CTD –*n* (%)	56 (9%)	12 (20%)	44 (8%)	0.042
RBBB – *n* (%)	40 (7%)	10 (17%)	30 (5%)	0.035
LBBB – *n* (%)	2 (0.3%)	0 (0%)	2 (0.4%)	>0.999

LAFB – *n* (%)	20 (3%)	4(7%)	16(3%)	0.256
QTc interval prolongation –*n* (%)	184 (30%)	36 (60%)	148 (27%)	0.001
PR interval	158 (26%)	4 (7%)	154(28%)	0.521
Pathological Q wave–*n* (%)	6 (2%)	1 (3%)	5 (2%)	0.464
ST-segment change – *n* (%)	48 (8%)	16 (27%)	32 (6%)	0.001
ST-segment elevation–*n* (%)	2 (0.3%)	0 (0%)	2 (0.4%)	>0.999
ST-segment depression–*n* (%)	46 (8%)	16 (27%)	30 (5%)	0.001
T-wave change – *n* (%)	184 (32%)	36 (60%)	148 (29%)	0.001
Inverted T-wave – *n* (%)	44 (7%)	8 (13%)	36 (7%)	0.251
Flat T-wave – *n* (%)	150 (25%)	28 (47%)	122 (22%)	0.006
Abnormal ECG point(s)	2 (0–2)	4 (1–4)	2 (0–2)	<0.001

- *Note*: Statistically significant p-values ($p < 0.05$) are shown in bold.
- Abbreviations: AF, atrial fibrillation; AVB, atrioventricular block; CTD, conduction tissue disease; LAFB, left anterior fascicular block; LBBB, left bundle branch block; RBBB, right bundle branch block.

As listed in Table-2, non-survivors had significantly longer QTc interval and higher rate of axis deviation, arrhythmias, conduction tissue disease, QTc interval prolongation, ST-segment change, and T-wave change. The PR interval and the proportion of atrioventricular block and pathological Q wave of the two groups were similar. Atrial fibrillation and sinus tachycardia were detected in 20 (3.3%) and 58 (9.5%) patients respectively and both of them were more common in non-survivors. First degree atrioventricular block (AVB) was seen in 20 patients (3.3%) and second degree AVB Mobitz type I was found in 4 patients (0.7%). The proportion of right bundle branch block was higher among non-survivors but left bundle branch block was not. Among patients with ST-segment change, the majority of them developed ST-segment depression (95.8%. 46/48) and only one patient developed ST-segment elevation. The proportion of flat T-wave was higher among non-survivors but inverted T-wave was not.

As shown in Figure-1, the proportion of abnormal ECG score from 0 point to 6 points was 38.6% (236 patients), 29.7% (182 patients), 19.3% (118 patients), 7.8% (48 patients), 2.9% (18 patients), 1.3% (8 patients), and 0.3% (2 patient), respectively. No patient had abnormal ECG score of 7 or 8 points. The median abnormal ECG score was significantly higher in non-survivor group (2.0[1.0,4.0] vs 1.0[0.0,2.0], $p < 0.001$). Table-2 summarized the electrocardiographic characteristics in detail.

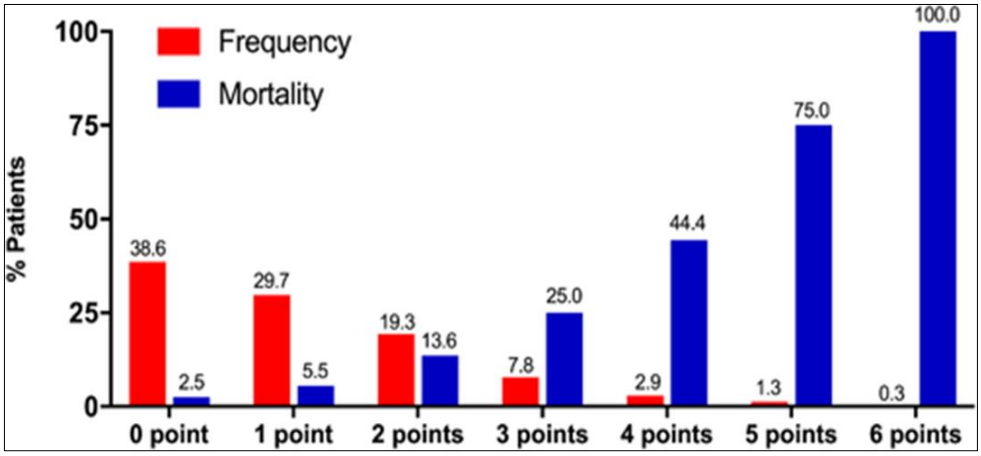

Fig 1

Frequency and mortality of patients with abnormal electrocardiography points from 0 to 6

Association between ECG findings and in-hospital mortality

The media duration of in-hospital stay was 22.00 (IQR, 12.75,29.00) days in all patients and was significantly shorter in non-survivors group (11.50 [IQR, 6.00,17.50] days vs 23.00 [IQR, 14.00,30.00] days, $p < 0.001$). The media duration of in-hospital stay was similar between patients with or without abnormal ECG point(s) (23.00 [IQR, 13.00,30.00] days vs 21.00 [IQR, 12.00,28.00] days, $p = 0.193$). During in-hospital follow-up, a total of 60 patients (9.8%) died and 552 patients (90.2%) were cured and discharged. As shown in Figure-1, the in-hospital mortality rate was 2.5% 5.5%, 13.6%, 25.0%, 44.4%, 75.0%, and 100.0% in patients with abnormal ECG points of from 0 to 6, respectively. Compared with patients without abnormal ECG point (0 point), the in-hospital mortality rate was higher among patients with abnormal ECG point(s) (≥1 points) (14.4% vs 2.5%, $p = 0.001$)

In multivariable Cox regression model 1, age, cardiac injury, abnormal ECG and comorbidities were associated with in-hospital mortality. After adjusting for age, cardiac injury, glucocorticoid treatment and mechanical ventilation, the multivariable Cox regression model 2 showed that in-hospital mortality was associated with abnormal ECG points (HR 1.478, 95% CI 1.131–1.933, per one point increase, $p = 0.004$) and age (HR 1.054, 95%CI 1.011–1.100, per year increase, $p = 0.014$), cardiac injury (HR 4.905, 95%CI 1.985–12.116, $p = 0.001$), and glucocorticoid treatment (HR 10.330, 95%CI 3.095–34.475, $p < 0.001$) were also independently associated with in-hospital mortality (Table -3).

Table 3: Univariable and multivariable Cox regression analysis

	Univariable regression analysis			Multivariable regression analysis		
Model 1	**HR**	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
1.Age	1.111	1.071–1.153	<0.001	1.062	1.021–1.105	0.003
2.Cardiac injury	15.620	7.114–34.295	<0.001	5.668	2.359–13.616	<0.001
3.Abnormal ECG	1.978	1.614–2.425	<0.001	1.479	1.121–1.950	0.006
Univariable regression analysis				Multivariable regression analysis		
Model 2	HR	95% CI	*p*-value	HR	95% CI	*p*-value
1.MV	12.744	5.154-31.507	<0.001	10.230	3.090-33.575	<0.001
2.Glucocorticoid	17.784	5.376–58.833	<0.001	10.330	3.095–34.475	<0.001
4.Comorbidities	4.128	1.572-10.837	0.004	1.479	10.757	0,006

- *Note*: Statistically significant *p*-values ($p < 0.05$) are shown in bold.
- Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; HR, hazard ratio; MV, mechanical ventilation; SBP, systolic blood pressure.

Discussion

This study evaluated the ECG findings at admission and thereafter during hospitalization to predict the prognosis in SARS-CoV-2 hospitalized patients. Our data showed that ECG is useful in identifying patients with a worse in-hospital clinical outcome. Repeated ECG can be a strong clinical tool to evaluate the adverse in-hospital outcome.

In our cohort, there was a significant association between abnormal ECG and major adverse events in patients with COVID-19. The abnormal ECG findings at admission, as a marker of heart disease, identify subgroups of patients with COVID-19 at a greater risk for adverse prognosis during the hospital stay. Therefore, serial ECG could help clinicians stratify the overall risk in COVID-19 patients, given the association between 7-day ECG alterations and the higher rate of intensive care, orotracheal intubation and renal replacement therapy

The main findings of our study are threefold: (a) Various abnormal ECG findings were common among patients with COVID-19; (b) Proportions of many ECG abnormalities were significantly higher in non-survivors; (c) Abnormal ECG was significantly associated with in-hospital mortality in COVID-19 patients after adjusting for potential confounding factors. Furthermore, per one point of abnormal ECG increasing was associated with a 47.8% increase in the relative risk of in-hospital mortality.

Abnormal ECGs were frequently encountered among COVID-19 patients. A recent study including 324 patients with COVID-19 had found that any abnormal finding on the ECG was found in 120 patients (37%) [9]. The proportion of abnormal ECG was as high as 93% among critical ill COVID-19 patients [8] Nearly two third of patients in our study had at least one point of ECG abnormalities scoring. Although ECG data of patients with pneumonia caused by non-SARS-CoV-2 pathogens was unavailable in our study, previous study had shown that ECG abnormalities prevalence were similar between COVID-19 and acute infectious respiratory disease caused by other pathogens (37.0% vs 43.5%, $p = 0.13$) and no differences in ECG abnormalities were found between the COVID-19 group and no-COVID-19 group [2, 6, 12].

Many studies in recent past had reported that atrial fibrillation, increasing heart rate, a QRS duration ≥110 ms (including patients with LBBB or RBBB) and ST-segment depression were associated with short term mortality of hospitalized COVID-19 patients in univariable Cox regression analysis [3, 7, 9]. The relation between abnormal ECG findings and in-hospital death of our present study was consistent with many studies done in recent past. We speculated that both of atrial fibrillation and increasing heart rate might result from hypoxia, fever and hyperinflammatory and ST segment change might be due to myocardial ischemia or injury. Bundle branch block and QRS lengthening indicated a delay in ventricular depolarization which might be explained by myocardial injury. Prevalence of incomplete RBBB and complete RBBB was 9% and 11% respectively in a large series of critically ill COVID-19 patients and the interpretation of such ECG abnormalities proposed by many studies in near past was right ventricular pressure overload [8] Due to the limited data of echocardiography in the present study, we did not explore the pathophysiological insights of RBBB.

A smaller series [13] including 50 COVID-19 patients had found that ST-T abnormalities were common (30%) at admission, which was comparable with our data. In a study of 107 patients hospitalized with COVID-19, first-degree AVB was seen in 20 (18.7%) patients and 1 (0.9%) patient developed transient Mobitz II AVB [7] First degree and second degree AVB were also seen in our study. This might suggest that conduction system could be involved by SARS-CoV-2 infection. The proportion of QTc interval prolongation was 30% in our study, which was in agreement with previous report with corresponding proportion of 38% [4, 5, 6, 8].QTc interval prolongation might be attributed to serious illness and hypoxemia.[8]

To the best of our knowledge, no study has so far evaluated the prevalence and clinical implications of QRS axis deviation in COVID-19 patients. Axis deviation was detected in 11% of patients in our study and was more often among non-survivors (33% vs 9%, $p<0.001$). Although the precise mechanism of axis deviation was largely unknown, axis deviation might be attributed to depolarization disorder, which could be seen in pulmonary hypertension, left ventricular hypertrophy and myocardial ischemia.

Cardiac injury defined as hs-cTnI elevation was common in COVID-19 patient and had been determined to be associated with mortality[2,3,6,7,8] Many reported that 19.7% of COVID-19 patients had cardiac injury and patients with cardiac injury were at a higher risk of death[3,9,10,11] In our present study, a total of 88 patients (14.4%) had cardiac injury and cardiac injury was independently associated with in-hospitalized mortality, which was in line with previous studies[12,13,14]. A recent study including 324 patients affected by COVID-19 had found that abnormal ECG was significantly associated with death when adjusted for cTnI levels in a minority of patients with available cTnI data.[9] Consistent with this finding, abnormal ECG showed significant association with mortality after adjusting for

cardiac injury and other relevant clinical and treatment variables in our large series of 612 patients with cTnI measurement. Importantly, our data indicated that relative risk of in-hospital mortality increased with increasing abnormal ECG scores. Abnormal ECG scores in our study reflected a wide spectrum of cardiac involvement including arrhythmias, conduction disorders and ventricular depolarization and repolarization disorders. The mechanisms of cardiovascular manifestations in COVID-19 patients remained unclear and several putative mechanisms had been proposed such as direct viral myocardial injury, stress cardiomyopathy, acute coronary syndrome, oxygen supply and demand mismatch and systemic hyperinflammatory response [16, 17, 18, 19] The increase of abnormal ECG scores might be attributed to severer acute cardiac complications of COVID-19 induced by multiple mechanisms and/or more pre-existing cardiovascular diseases. Complications and poor outcomes more frequently occurred in elderly COVID-19 patients [11, 15, 20, 21, 22]. Consistent with these findings, increasing age was independently associated with in-hospital death in the present study. An unexpected finding was that treatment with glucocorticoid was also related to mortality in multivariable Cox regression analysis. A possible explanation might be that serious patients tended to receive glucocorticoid therapy[15] and non-survivors also was with a higher proportion of glucocorticoid therapy [11, 23, 24].

Conclusion

Our data showed that ECG abnormality was common among admitted patients for COVID-19 and was associated with adverse in-hospital outcome. In-hospital mortality risk increased with increasing abnormal ECG scores, suggesting that close observation should be kept on patients with multiple ECG abnormalities during their hospitalization. ECG might be an easy tool for risk stratification in such patients. Our study evaluated the role of serial ECG findings in hospitalized patients with COVID-19. ECG alterations at admission and even more subsequent ECG findings at 7-day ECG could help the clinicians stratify the risk of major adverse events in COVID-19. Serial ECG recordings can track the unfavorable course of patients with COVID-19. Indeed, ECG alterations were closely linked with the severity of the SARS-Coronavirus-2 infection and could express a direct or indirect cardiac involvement related to the physiopathological mechanism of this complex disease.

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Conflict of Interest

All authors declare no conflicts of interest that might be relevant to the contents of this manuscript.

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