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Importance of ECG findings in COVID-19 patients: Predictor of in-hospital prognosis

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Original Article

Abstract

BACKGROUND: Cardiac injury in COVID-19 patients confers a worse prognosis. The interpretation of electrocardiography can be beneficial in the early diagnosis of probable cardiac involvement. After adjusting for other variables, we sought to determine if the initial ECG on admission could add additional prognostic value.

METHODS: In this single-center cross-sectional study, 1165 patients with a positive COVID-19 PCR between Feb 2020 and Nov 2021 were enrolled in our study. Patients were grouped according to their admitted units, and survivors to hospital discharge or non-survivors. Predictors of ICU admission and in-hospital mortality were determined using univariate analysis and a logistic regression model.

RESULTS: The mean age was 55.6 ± 16.2 years and 52% were male. Out of 1165 patients, 149 deaths (12.8%) were recorded during hospitalization. Sinus tachycardia was the most common dysrhythmia, followed by premature atrial and ventricular beats, sinus bradycardia, and atrial fibrillation (28.6%, 5.6%, 3.9%, and 2.1%, respectively). Age (p<0.001), sex (p=0.006), history of diabetes mellitus (p=0.002), hypertension (p=0.018), ischemic heart disease (p=0.004), and cancer (p<0.001) were more frequent among non-survivors. Among ECG findings, tachycardia, low voltage QRS, ST-T changes, and dysrhythmia were related to an increased mortality risk. However, in regression analysis, only sex (OR 1.89, 95% CI 1.2 to 2.9, p=0.004), age (OR 1.03, 95% CI 1.02 to 1.05, p<0.001), and initial tachycardia (OR 1.02, 95% CI 1.01 to 1.03, p<0.001) were independent predictors of in-hospital mortality.

CONCLUSION: Our data suggest that initial electrocardiographic findings could be helpful in distinguishing patients with an increased risk for ICU admission or in-hospital death.

Keywords: Electrocardiography; COVID-19; Mortality; ICU Admission; Predictors

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Introduction

Coronavirus disease 2019 (COVID-19), which emerged from Wuhan, China in December 2019 and was declared a pandemic by the WHO on March 11, 2020, is a highly contagious disease affecting millions of people worldwide[1]. Cardiac injury in COVID-19 patients confers a worse prognosis, even in the absence of pre-existing cardiovascular disease. However, early identification of an at-risk population remains challenging[2, 3].

Electrocardiography ECG interpretation can be beneficial in the early diagnosis of probable cardiac involvement, with at least one abnormality seen in up to 90% of critically ill patients. Cardiac involvement in these subjects could result from cytokine storm, hypoxic injury, electrolyte disturbances, acute myocardial injury, or coronary micro thrombi or spasm[4, 5].

While sinus tachycardia and repolarization abnormalities are thought to be the most common ECG findings among COVID-19 cases, supraventricular and ventricular arrhythmias, along

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with various bradycardias, interval or axis changes, and ST-T disturbances may frequently be observed in hospitalized patients[5,6].

To date, several prognostic factors have been addressed in different studies as markers of poor outcome and increased mortality. In a study of 1258 COVID-19 positive patients, the combination of abnormal respiratory vital signs and ECG findings of atrial fibrillation/flutter, right ventricular strain, or ST segment abnormalities were suggested as predictors of early deterioration of hospitalized patients[7]. According to another paper of 265 patients presenting to the emergency departments of French hospitals, the presence of axis deviation and left bundle branch block on initial ECG were associated with an increased risk of in-hospital mortality[6].

Other clinical and electrocardiographic variables mentioned as prognostic markers of mortality in relatively small sample-size studies were male sex, higher age, diabetes mellitus, low QRS voltage criteria, QRS and QT prolongation, presence of PVC or PACs, pulmonale P wave, QT dispersion, left ventricular hypertrophy, RBBB, and heart rate above 100 beat/min[8-11]. Nevertheless, in a meta-analysis of limited few studies on bradycardia, no significant correlation was found between initial low heart rate and increased mortality in COVID-19 patients[12].

To date, only a few large-scale studies have analyzed the prognostic value of initial electrocardiogram findings. Given the high volume of hospitalized patients with SARS-CoV-2 in our hospital from the beginning of this pandemic, we sought to determine if the initial ECG on admission could add additional prognostic value after adjusting for other variables such as age, sex, comorbidities, and initial vital signs.

Methods

Study design and population

This is a single-center cross-sectional study conducted at a referral center for COVID-19 patients from the beginning of the pandemic. All patients over 15 years of age with a positive nasopharyngeal swab test for real-time COVID-19 PCR (polymerase chain reaction) between Feb 2020 and Nov 2021 were enrolled in our study. Out of 3521 subjects admitted to the hospital wards or intensive care units (ICU), 1230 had an initial ECG taken at their admission time. Patients recently treated with drugs potentially affecting cardiac intervals such as digoxin, hydroxychloroquine, specific antimicrobial and antidepressant agents, as well as patients dying from disorders other than COVID-19 related complications (e.g., active cancer) during their hospital stay, were excluded, leading to 1165 cases meeting the proposed criteria.

Data consisted of patients' demographics, comorbidities (including hypertension, diabetes mellitus, chronic heart failure, ischemic heart disease, chronic kidney disease), social history (cigarette smoking or addiction), initial vital signs (blood pressure, heart rate, respiratory rate, oxygen saturation and body temperature) and duration of hospital stay were extracted from medical records. Subjects were grouped according to their admitted units (ICU or general wards), as well as survivors to hospital discharge or non-survivors.

The criteria used for ICU admission were as follows: 1) respiratory rate more than 30, 2) oxygen saturation below 90%, 3) respiratory distress needing endotracheal intubation, 4) hypotension (systolic blood pressure below 90 mmHg), 5) acute organ dysfunction (e.g., confusion, liver or renal injury), 6) significant cardiac arrhythmias, 7) elevated biomarkers of myocardial injury (i.e., troponin and NT-pro BNP).

ECG analysis and definitions

Standard 12-lead ECGs taken within the first 24 hours of admission were manually analyzed by an emergency physician and a specialized cardiologist, both of whom were blinded to the study outcomes. A 200 percent magnification was applied for the interpretation of intervals. Cardiac rhythm, rate, and axis, along with atrioventricular or intraventricular conduction parameters (including AV blocks, bundle branch blocks, or hemi blocks) and repolarization abnormalities (corrected QT interval, ST segment, and T wave changes) were recorded for each patient.

Tachycardia and bradycardia were defined as a heart rate >100 and <60 beats/min, respectively. A T wave inversion was defined as a negative T wave with more than 0.1 mV amplitude in limb or precordial leads, except for lead III, AVR, and V1. ST segment changes were considered significant if at least a 1 mm deviation was detected from the isoelectric line. The corrected QT interval (QTc) was calculated

according to the Hodge formula:

$$QTc=QT+1.75\times(\text{heart rate}-60)$$

and prolonged QTc was defined as values above 440 msec in men and 460 msec in women.

For QRS duration, values equal to or more than 120 msec were considered wide and reported as right (RBBB) or left bundle branch block (LBBB) or intraventricular conduction delay (IVCD). Low amplitude QRS (LoQRS) was defined as the composite of either QRS amplitude less than 5 mm in limb leads or 10 mm in precordial lead. Arrhythmias observed in our study were atrial or ventricular premature beats, atrial fibrillation, multifocal atrial tachycardia, AV nodal reentrant tachycardia, and ventricular tachycardia.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation and were compared using the Student's t-test and ANOVA test. Categorical variables are expressed as numbers (%) and were compared using the Chi-square or Fisher's exact test, as appropriate.

To evaluate the relationship between baseline variables and ECG findings with ICU admission and in-hospital mortality, we first placed each variable in a dataset separately using univariate analysis. Then, we entered all variables with a probable relationship with ICU admission and mortality ($p<0.1$) into the binary logistic regression model using the stepwise backward method, in order to identify the prognostic factors of ICU admission and in-hospital mortality. The odds ratio (OR) and confidence interval (CI) were calculated for each independent parameter, and a p-value of <0.05 was considered significant. All analyses were performed using IBM SPSS software for Windows, version 22.

Results

Baseline characteristics

A total of 1165 patients with a positive COVID-19 PCR were included in this study (Figure 1). The

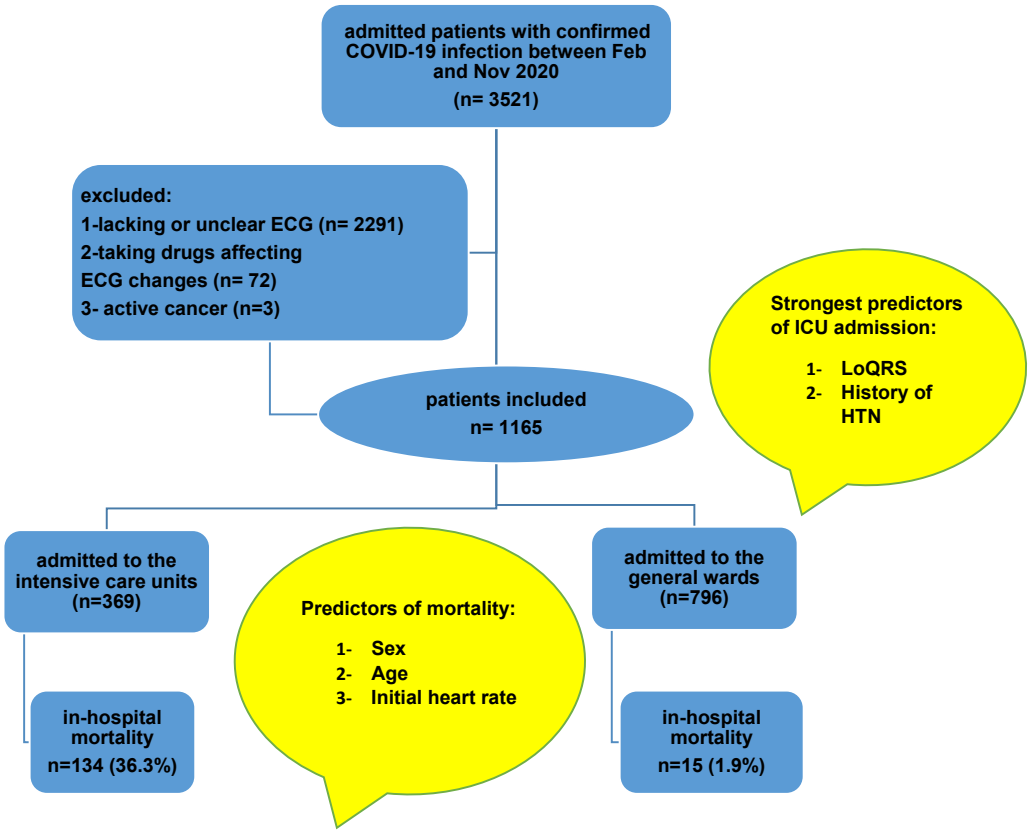

Figure 1. Graphical abstract

mean age was 55.6 ± 16.2 years, and 612 were male. During hospitalization, 149 patients died, accounting for a mortality rate of 12.8%. The median length of hospital stay was 7.6 days, and 369 patients (31.6%) were admitted to the critical care units. Among the ICU-admitted patients, 134 (36.3%) died, while 15 subjects (1.9%) who were admitted to the general wards died during hospitalization.

Most of the admitted patients were nonsmokers (95.4%), and 68.7% had at least one medical problem. Hypertension, diabetes, and ischemic heart disease were the most frequent underlying conditions, with prevalences of 30%, 17.8%, and 12.2%, respectively.

Initial vital signs were also extracted from hospital medical records. Upon arrival, 476 subjects (40%) were febrile (daytime body temperature > 37.3 degrees), whereas 104 (8.9%) had relative hypothermia (T<36°). Severe hyperthermia, defined as T>39°, was detected in 28 (2.4%) patients. Most cases had normal initial respiratory rate and blood pressure (59.4% and 76.8%, respectively).

Clinical and electrocardiographic findings in ICU and general ward admitted patients

In our study, sinus tachycardia was the most common dysrhythmia, followed by premature atrial/ventricular beats, sinus bradycardia, and atrial fibrillation (28.6%, 5.6%, 3.9%, and 2.1%, respectively). We recorded only one case of sustained ventricular tachycardia (VT) as the initial rhythm of a 66-year-old diabetic male who did not survive after resuscitation. Non-sustained VT (duration <30 sec) was detected in two patients on their admission ECG, among which one survived to hospital discharge, while the other died in the ICU. AV block was detected in 24 patients (2%), primarily in the form of grade-1 AV block; however, we observed only one case of complete heart block who died despite the emergent placement of a temporary intravenous pacemaker.

The baseline average QT interval duration was 388 ± 32.8 msec, and a prolonged QT interval was observed in 65 patients (5.6%). Wide QRS was found in 38 cases (3.3%), and 951 patients (81.6%) did not show significant ST-T changes on their admission ECG. However, ST-elevation myocardial infarction occurred in 15 cases as the primary presentation on admission. Axis deviation and LoQRS were observed in 197 (16%) and 405 (34.7%) subjects, respectively.

Table 1 illustrates the baseline characteristics and electrocardiographic variables of the two groups, and factors associated with an increased risk of ICU admission were evaluated using univariate and logistic regression analyses (Table 2). Those admitted to the intensive care units were significantly older, had more underlying illnesses, and worse initial vital signs (higher body temperature, respiratory and heart rate, and lower oxygen saturation). In univariate analysis, the presence of axis deviation (p=0.01), any kind of dysrhythmia (p=0.001), ST-T changes (p<0.001), heart blocks (p<0.001), QT prolongation (p=0.007), and precordial lead low voltage (p=0.03) were observed significantly more frequently in ICU-admitted patients. However, there were no significant differences in QRS duration and limb lead low voltage between ICU and general ward-admitted patients (p=0.142 and 0.16, respectively). Interestingly, in logistic regression analysis, the presence of precordial limb low voltage [OR=1.64 (1.07-2.5), p=0.02] and history of hypertension [OR= 1.5 (1.12-2.15), p=0.008] were the strongest predictors of ICU admission after adjusting for other clinical and electrocardiographic variables. As illustrated in Table 2, other independent predictors of ICU admission were prolonged QT interval [OR= 0.99 (0.98-0.99), p<0.001], tachycardia [OR=0.99 (0.98-0.99), p=0.023], older age [OR=0.98 (0.97-0.99), p=0.001], and higher body temperature [OR=0.73 (0.61-0.87), p<0.001].

Clinical and electrocardiographic factors associated with in-hospital mortality

To compare different variables between surviving and deceased patients, we utilized univariate analysis and a logistic regression model (Table 3 and Table 4). In univariate analysis, age (p<0.001), sex (p=0.006), history of diabetes mellitus (p=0.002), hypertension (p=0.018), ischemic heart disease (p=0.004), and cancer (p<0.001) were more frequent among non-survivors. However, congestive heart failure, chronic kidney disease, and obstructive pulmonary disease were not significantly different between survivors and non-survivors (p=0.127, 0.90, and 0.142, respectively). Although initial tachypnea, high blood pressure (above 120 mmHg), and tachycardia were associated with a higher risk of mortality (p<0.001, 0.002, and <0.001, respectively), there was no significant difference across the groups in terms of high body temperature or positive social history (p=0.09 and 0.64, respectively).

Table 1. Baseline characteristics and electrocardiographic variables in ICU and general ward admitted patients.

		ICU(n=369)	General ward(n=796)	Overall (n=1165)	P value
Age		61.24 (±16.8)	53.07(±15.25)	55.66(±16.2)	<0.001
sex	**male**	208(56.4%)	404(50.8%)	612(52.5%)	0.074
	female	161(43.6%)	392(49.2%)	553(47.5%)	
Smoking/addiction		21(5.7%)	33(4.1%)	54(4.6%)	0.24
Oxygen saturation		84.05(±11.8)	91.86(±5.2)	89.39(±8.7)	<0.001
Heart rate		91(±23)	85(±18)	87(±19)	<0.001
Respiratory rate		19(±4)	18(±2)	18(±3)	<0.001
Body temperature		37.34(±0.89)	37.09(±1.35)	37.1(±1.2)	<0.001
Blood pressure on admission above 120 mmHg		121(32.8%)	149(18.7%)	270(23.2%)	<0.001
Tachycardia		85(23%)	112(14.1%)	197(16.9%)	0.001
Wide QRS		16(4.3%)	22(2.8%)	38(3.3%)	0.012
QT duration(msec)		394(±36)	385(±31)	388(±32.8)	<0.001
QT prolongation		32(8.7%)	33(4.1%)	65(5.6%)	0.007
LoQRS		147(39.8%)	258(32.4%)	405(34.7%)	0.109
Low voltage leads	**Limb**	87(23.6%)	159(20%)	246(21.1%)	0.161
	Precordial	57(15.5%)	88(11.1%)	145(12.4%)	0.033
	Transient	3(0.8%)	11(1.4%)	14(1.2%)	0.567
ST-T changes	**ST depression or T inversion**	91(24.6%)	108(13.6%)	199(17.1%)	<0.001
	ST elevation (Myocardial infarction)	8(2.2%)	7(0.9%)	15(1.3%)	
Heart block	**Complete or incomplete LBBB**	24(6.5%)	15(1.9%)	39(3.3%)	<0.001
	Complete or incomplete RBBB	21(5.7%)	26(3.3%)	47(4%)	
	LAHB	18(4.9%)	29(3.6%)	47(4%)	
	AV block	10(2.7%)	14(1.7%)	24(2%)	
Axis deviation		80(21.7%)	117(14.7%)	197(16.9%)	0.013
Dysrhythmias: Sinus tachycardia		121(32.8%)	212(26.6%)	333(28.6%)	0.001
Sinus bradycardia		13(3.5%)	32(4%)	45(3.9%)	
Atrial fibrillation		14(3.8%)	11(1.4%)	25(2.1%)	
MAT		5(1.3%)	0(0%)	5(0.42%)	
PAC/PVC		37(10%)	28(3.5%)	65(5.57%)	
VT/NSVT		2(0.5%)	1(0.1%)	3(0.25%)	
AVNRT		1(0.2%)	1(0.1%)	2(0.17%)	
History of Diabetes		89(24.1%)	118(14.8%)	207(17.8%)	<0.001
History of hypertension		147(39.8%)	209(26.3%)	356(30.5%)	<0.001
History of Ischemic heart disease		62(16.8%)	80(10.1%)	142(12.2%)	0.001
History of Congestive heart failure		15(4.1%)	6(0.8%)	21(1.8%)	<0.001
History of cancer		11(3%)	9(1.1%)	20(1.7%)	0.024
History of Obstructive lung disease		17(4.6%)	16(2%)	33(2.8%)	0.013
History of Chronic kidney disease		14(3.8%)	8(1%)	22(1.9%)	0.001
death		134(36.3%)	15(1.9%)	149(12.8%)	<0.001

continuous and categorical variables were analyzed using Student's t-test and Chi-square methods, respectively; ICU: intensive care unit, LoQRS: low voltage QRS, LBBB: left bundle branch block, RBBB: right bundle branch block, LAHB: left anterior hemi block, AV: atrioventricular, MAT: multifocal atrial tachycardia, PAC: premature atrial contraction, PVC: premature ventricular contraction, VT: ventricul tachycardia, NSVT: non-sustained ventricular tachycardia, AVNRT: AV nodal reentrant tachycardia.

Table 2. Predictors of ICU admission based on logistic regression analysis

variable	OR	(95% CI)	P value
Age	0.98	0.97-0.99	0.001
Heart rate	0.99	0.98-0.99	0.023
Body temperature	0.73	0.61-0.87	<0.001
QT interval	0.99	0.98-0.99	<0.001
History of hypertension	1.5	1.12-2.15	0.008
LoQRS(precordial)	1.64	1.07-2.53	0.022

ICU: intensive care unit, LoQRS: low voltage QRS

Table 3. Univariate analysis of baseline characteristics and electrocardiographic variables in survivors and non-survivors groups.

		Non-survivors (n=149)	Survivors (n=1016)	P value
Age(mean)		66	54	<0.001
sex	**male**	94(63.1%)	518(51%)	0.006
	female	55(36.9%)	498(49%)	
Treating department	**ICU**	134(89.9%)	235(23.1%)	<0.001
	Ward	15(10.1%)	781(26.9%)	
Smoking/addiction		8(5.4%)	46(4.5%)	0.648
Oxygen saturation		79.6(±14.3)	90.8(±6.4)	<0.001
Tachypnea		90(60.4%)	375(36.9%)	<0.001
Body temperature		37.3(±0.9)	37.15(±1.2)	0.091
Blood pressure on admission above 120 mmHg		52(34.9%)	217(21.3%)	0.002
Tachycardia		47(31.5%)	150(14.8%)	<0.001
Wide QRS		3(2%)	35(3.4%)	0.358
QT duration(msec)		393(±33)	387(±32)	0.041
QT prolongation		10(6.7%)	55(5.4%)	0.478
LoQRS		70(46.9%)	335(32.9%)	0.005
Low voltage leads	**Limb**	45(30.2%	201(19.8%)	0.004
	Precordial	24(16.2%)	121(11.9%)	0.142
	Transient	1(0.7%)	13(1.3%)	0.99
ST-T changes	**ST depression or T inversion**	40(26.9%)	159(15.7%)	0.02
	ST elevation (Myocardial infarction)	2(1.3%)	13(1.3%)	
Heart block	**Complete or incomplete LBBB**	8(5.4%)	27(2.7%)	0.092
	Complete or incomplete RBBB	9(6%)	38(3.7%)	
	LAHB	9(6%)	38(3.7%)	
	AV block	5(3.3%)	19(1.8%)	
Axis deviation		35(23.4%)	162(15.9%)	0.135
Dysrhythmias: Sinus tachycardia		56(37.6%)	277(27.3%)	<0.001
Sinus bradycardia		3(2%)	42(4.1%)	
Atrial fibrillation		6(4%)	19(1.9%)	
MAT		5(3.3%)	0	
PAC/PVC		18(12.1%)	47(4.7%)	
VT/NSVT		2(1.3%)	1(0.1%)	
AVNRT		1(0.7%)	1(0.1%)	
History of Diabetes		40(26.8%)	167(16.4%)	0.002
History of hypertension		58(38.9%)	298(29.3%)	0.018
History of Ischemic heart disease		29(19.5%)	113(11.1%)	0.004
History of Congestive heart failure		5(3.4%)	16(1.6%)	0.127
History of cancer		8(5.4%)	12(1.2%)	<0.001
History of Obstructive lung disease		7(4.7%)	26(2.6%)	0.142
History of Chronic kidney disease		3(2%)	19(1.9%)	0.90

continuous and categorical variables were analyzed using Student's t-test and Chi-square methods, respectively; ICU: intensive care unit, LoQRS: low voltage QRS, LBBB: left bundle branch block, RBBB: right bundle branch block, LAHB: left anterior hemi block, AV: atrioventricular, MAT: multifocal atrial tachycardia, PAC: premature atrial contraction, PVC: premature ventricular contraction, VT: ventricular tachycardia, NSVT: non-sustained ventricular tachycardia, AVNRT: AV nodal reentrant tachycardia.

Table 4. Predictors of in hospital mortality based on logistic regression model

variable	OR	(95% CI)	P value
Sex (Male)	1.89	1.23-2.9	0.004
Age[1]	1.03	1.02-1.05	<0.001
Tachycardia[2]	1.02	1.01-1.03	<0.001

[1]Odds ratio is 1.03 for each year increase in age
[2]Tachycardia: heart rate above 100 beat/min

Non-survivors had a significantly higher prevalence of dysrhythmia (p<0.001) and ST-T changes (p=0.018), and the average QT interval duration was higher in this group. However, QRS duration, axis deviation, and the presence of heart blocks and prolonged QT interval were not different between the groups. Low amplitude QRS (LoQRS) was associated with a higher risk of mortality in univariate analysis (p=0.005), but in the binary logistic regression model, it was not found to be an independent predictor of in-hospital mortality.

Sinus tachycardia (37.6% vs 27.3%) and atrial fibrillation (4% vs 1.9%) were more common among non-survivors, and interestingly, all five patients with an initial rhythm of multifocal atrial tachycardia died within a few days. However, patients with initial lower heart rates or sinus bradycardia more frequently survived to hospital discharge (4.1% vs 2%). Despite the significant correlations of discussed factors and in-hospital mortality, in regression analysis only male sex [OR=1.89 (1.2-2.9), p=0.004], older age [OR=1.03 (1.02-1.05), p<0.001], and tachycardia [OR=1.02 (1.01-1.03), p<0.001] were found to predict in-hospital mortality (Table 4).

Discussion

This study is one of the largest single-center retrospective studies to evaluate the prevalence and significance of electrocardiographic changes in hospitalized COVID-19 patients. In addition, we analyzed baseline clinical and demographic features that may influence mortality and ICU admission of patients. Considering the rapidly evolving situation and decreasing fatality rate of the disease after worldwide vaccination programs, we found a mortality rate of 12.8% in our hospitalized cases, which was similar to that seen in Moreno Torres V, et al.'s study in Madrid during March 2020 and April 2021 before the vaccination era[13].

Approximately one-third of our cases were admitted to the intensive care units, with almost a thirty percent mortality rate in these critically ill patients. Two-thirds of all subjects had some kind of medical illnesses, among which hypertension, diabetes, and ischemic heart disease were the most prevalent risk factors, in line with other previous reports[6,9,14]. While the mentioned underlying conditions contributed to the higher risk of in-hospital mortality in univariate analysis, the history of congestive heart failure, chronic kidney disease, and obstructive pulmonary disease were not significantly different between expired and recovered patients. However, in the logistic regression model, none of the underlying medical conditions independently predicted in-hospital mortality. These findings should be interpreted with caution due to the relatively low prevalence of these illnesses and the fact that we didn't include the laboratory and echocardiographic data in this study, which was one of our limitations.

In contrast to prior reports[8], our subjects were less febrile, and about 10% showed significant hypothermia. Although this study was somewhat in line with other previous studies showing a significant correlation between in-hospital mortality and tachypnea, hypoxia, and high blood pressure on admission[15,16], none of these initial vital signs were independent predictors of mortality after adjusting for other variables, except for tachycardia. The larger sample size of our study may explain the differences, while more large-scale multicenter cohorts are needed to confirm our concept.

In terms of ECG changes in COVID-19 cases, we reported a 5.6% prevalence of prolonged QT interval on admission, a frequency similar to that in Rahel Mahmud's study on patients with acute medical admissions [17]. Although long QT intervals and the presence of axis deviation were more frequently seen in our ICU-admitted subjects, we didn't detect any significant correlation between QT or QRS duration and the risk of mortality, in contrast to the study by Harbalıoğlu H. and colleagues [9]. Our study population size and the exclusion of patients on medications affecting cardiac intervals before ECG interpretation may explain these contradictions. Considering these findings, we can propose that COVID-19 alone may not have a further effect on the QT interval, and medications used to treat these patients, as well as electrolyte disturbances resulting from gastrointestinal complications, could contribute to QT prolongation.

Another assumed cardiac complication of COVID-19 is the higher risk of ST-elevation myocardial infarction (STEMI), which is addressed as a late event in some previous records [18,19]. However, we found it an early presentation in only 1.2% of our subjects, indicating that plaque rupture and thrombus formation can occur even in the

very early phase of the disease as a consequence of increased sympathetic drive, systemic inflammatory response, or direct effects of viral toxins on the cardiovascular system. Long-term follow-up data on the real incidence of myocardial infarction is missing in our study due to its retrospective nature; besides, we have only included acute ST-elevation myocardial infarctions based on admission ECG. But other large analytical studies agree that COVID-19 could be an important risk factor for myocardial infarction, with a 1.6 to 2.8 fold increased relative risk during the first month of infection [20,21].

Similar mechanisms of direct toxin effects on conduction systems, beyond the disturbance of neuro-hormonal activity, may contribute to the increased risk of heart blocks and conduction abnormalities in affected patients. In line with our prior case review on the occurrence of complete heart block (CHB) in SARS-COV-2 cases [22], and despite a two percent prevalence of atrioventricular block detected in the present study, CHB was observed only in one patient who didn't survive to hospital discharge, suggesting its rare and ominous nature. Another potentially malignant rhythm addressed in our study was multifocal atrial tachycardia, which was seen exclusively in non-survivors. Despite these expected findings, initial sinus bradycardia and low heart rates - although not significantly different - were interestingly more frequent in recovered patients (4% vs 3.5%), challenging the concept of Amaratunga EA's literature, which proposed the hypothesis that relative bradycardia could be linked to later disease progression and cytokine storm [23]. Whether an increased level of pro-inflammatory markers in studied patients contributed to this adverse outcome, or it was merely due to the unwanted effects of medications used for infection treatment, is not clear. However, considering our sample volume, we can suggest that non-complex bradycardias could be protective via their counter-regulatory effects on sympathetic and cytokine storms, but the precise mechanism remains unknown and needs further investigation.

In our literature, sinus tachycardia and atrial fibrillation were more commonly found in expired cases, and an increased heart rate on admission was the only independent predictor of in-hospital mortality among ECG findings. Although the presence of 24.3% low voltage QRS was proposed to be attributed to the high incidence of in-hospital mortality in the study of J Lampert and colleagues in COVID-19 cases [24], we didn't find it an independent predictor of in-hospital mortality after adjusting for other variables, despite its high prevalence (34.7%). Various clinical conditions can affect the presence of low voltage QRS, and the lack of information about patients' body mass index, body fat area, the presence of pleural or pericardial effusion, or possible underlying lung disease in both studies may influence the results. Therefore, future research should be planned to eliminate these confounding factors to address the significance of LoQRS in COVID-19 patients.

Similar to previous studies, older age and male sex were the most important predictors of in-hospital mortality. In the study of Kaliyaperumal D. and colleagues on 315 hospitalized COVID-19 cases, ischemic ST-T changes were associated with respiratory failure [25]. However, in line with Pinto-Filho MM. et al.'s literature, we found that only initial tachycardia is an independent predictor of mortality after adjusting for other variables [26].

Limitations

Our study had some limitations. First, we enrolled patients who had an initial ECG on their admission day records. Moreover, ECG was not routinely obtained during the first months of the COVID-19 pandemic, and many critically ill patients might have had ECG abnormalities that were missed due to the lack of continuous cardiac monitoring, high volume of referral cases, and insufficient facilities. Second, we did not evaluate the ECG changes during hospitalization. As we only included the initial electrocardiographic data, transient possible disturbances before the clinical worsening of deceased patients were missing in our literature. These limitations could also explain the low incidence of malignant arrhythmias as well as significant ST-T changes in our study. Finally, the absence of laboratory and imaging data affects our predictors of mortality, which can be addressed in future studies.

Considering all the above findings, we agree that ECG changes during the COVID-19 era may represent underlying cardiac involvement and could help further risk assessment of patients. Nevertheless, before the availability of convincing evidence from further research, none of these findings should be

interpreted as independent markers of mortality, while patients' age, alongside comorbidities and other clinical factors, may still play an important role in the risk assessment of these cases.

Conclusion

We evaluated the prevalence and significance of baseline ECG abnormalities, in addition to clinical factors and demographic features, in a large group of COVID-19 patients in our center. Our data suggest that although older age, male sex, decreased oxygen saturation, tachypnea, tachycardia, the presence of low voltage QRS, ST-T changes, and dysrhythmia correlate with an increased risk of in-hospital mortality, only the patient's age, sex, and tachycardia on admission were independent predictors of mortality after adjusting for other variables.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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Author's Contributions

MB, principal investigator of the study, designed the study. MM cooperated in collecting medical reports and initial data.VA analyzed the data. MB wrote the draft and finalized the manuscript. All authors read and approved the manuscript.

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