Association of Electrocardiographic Abnormalities With In-hospital Mortality in Adult Patients With COVID-19 Infection

Published online: 11 November 2024
https://doi.org/10.69944/pjc.5c582949d3
https://pjc.philheart.org
ISSN: 0115-1029
e-ISSN: 2815-2123
Volume 52 Issue 2

Jannah Lee Tarranza, MD* | Marcellus Francis Ramirez, MD*† | Milagros Yamamoto, MD*
* Section of Adult Cardiology, Department of Internal Medicine, University of Santo Tomas Hospital, Manila, Metro Manila, Philippines
† Division of Electrophysiology, Section of Adult Cardiology, Department of Internal Medicine, University of Santo Tomas Hospital, Manila, Metro Manila, Philippines

Correspondence:
Jannah Lee Tarranza, MD
E-mail: jannahleetarranza@gmail.com

CONFLICTS OF INTEREST: None

Abstract

OBJECTIVES: The study aimed to determine the association of electrocardiographic (ECG) abnormalities and in-hospital mortality of patients with coronavirus disease 2019 (COVID-19) infection admitted in a tertiary care hospital in the Philippines.

METHODS: We conducted a retrospective study of confirmed COVID-19–infected patients. Demographic and clinical characteristics and clinical outcomes were extracted from the medical records. Electrocardiographic analysis was derived from the 12-lead electrocardiogram recorded upon admission. The frequencies and distributions of various clinical characteristics were described, and the ECG abnormalities associated with in-hospital mortality were investigated.

RESULTS: A total of 163 patients were included in the study; most were female (52.7%) with a median age of 55 years. Sinus rhythm with any ECG abnormality (65%), nonspecific ST and T-wave changes (35%), and sinus tachycardia (22%) were the frequently reported ECG findings. The presence of any ECG abnormality was detected in 78.5% of patients, and it was significantly associated with in-hospital mortality ($P = 0.038$). The analysis revealed a statistically significant association between in-hospital mortality and having atrial fibrillation or flutter ($P = 0.002$), supraventricular tachycardia ($P = 0.011$), ventricular tachycardia ($P = 0.011$), third-degree atrioventricular block ($P = 0.011$), T-wave inversion ($P = 0.005$), and right ventricular hypertrophy ($P = 0.011$).

CONCLUSION: The presence of any ECG abnormality in patients with COVID-19 infection was associated with in-hospital mortality. Electrocardiographic abnormalities that were associated with mortality were atrial fibrillation or flutter, supraventricular tachycardia, ventricular tachycardia, third-degree atrioventricular block, T-wave inversion, and right ventricular hypertrophy.

KEYWORDS: COVID-19, electrocardiography, mortality, Philippines

INTRODUCTION

The 2019 novel coronavirus disease (COVID-19) caused by a highly infectious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a worldwide, rapidly spreading, and high-mortality pandemic. As of December 2023, the World Health Organization reported a total of 772 million confirmed COVID-19 cases and nearly 7 million confirmed deaths worldwide.[1] The Philippines' Department of Health reported a total of 4.13 million confirmed COVID-19 cases with 66,813 deaths.[2]

SARS-CoV-2 is mainly a respiratory virus that is primarily transmitted through respiratory droplets, either by direct or indirect contact with nasal, conjunctival, or oral mucosa when respiratory particles are inhaled or deposited on these mucous membranes. The conjunctiva and gastrointestinal tract are also susceptible to infection and may serve as transmission portals.[3–5] A systematic review by Macedo et al[6] reported that the overall mortality rate for COVID-19 patients admitted to hospitals was 17% to 20%,[7] with acute respiratory distress

syndrome (ARDS) being the most common cause of death.[7] Likewise, a similar mortality rate of 17.5% was reported by Salamat et al[8] in the Philippines.

Several studies reported that underlying cardiovascular diseases (CVDs), such as hypertension, obesity, coronary artery disease, and congestive heart failure, are identified risk factors of mortality among COVID-19 patients.[9–11] Cardiometabolic changes and multiorgan dysfunction are among the problems that have been reported following COVID-19 pneumonia, thereby aggravating the disease and increasing the probability of mortality.[5,12] COVID-19 can directly or indirectly affect the cardiovascular system and lead to myocarditis, myocardial infarction, and thromboembolism[13–16] and a range of electrocardiographic (ECG) abnormalities.[12,16–20]

A significant marker for severe COVID-19 is myocardial injury, which can be detected through electrocardiography.[21] The electrocardiogram remains the simplest and most useful screening tool in recognizing myocardial injury or rhythm alterations in patients with COVID-19. Electrocardiographic abnormalities were described in 15% to 37% of cases in various studies.[8,12,20] However, there is a paucity of data in the Philippines, and there have been neither large studies of ECG abnormalities in COVID-19 patients nor their correlation with clinical outcomes.

Electrocardiographic abnormalities, whether they indicate an underlying cardiac illness or are a complication of the infection, can underline its clinical impact on outcomes in COVID-19 patients. It helps in the identification of patients at increased risk of a negative in-hospital clinical outcome. More importantly, the study may provide information on the patient's prognosis and guidance on the future management of patients with COVID-19 infection in the hope of reducing mortality from cardiac complications. Therefore, this study was designed to determine the ECG abnormalities and its correlation with in-hospital mortality of COVID-19 patients.

METHODOLOGY

This study was a retrospective observational study of COVID-19 patients admitted at the University of Santo Tomas Hospital, a tertiary care hospital in Manila, Philippines. A total enumeration of COVID-19 patients admitted from March 2020 until December 2021 was considered for inclusion in this study.

Inclusion and Exclusion Criteria

Patients included should satisfy all the following criteria:

Inclusion criteria

- Adult patients 18 years or older
- Confirmed COVID-19 cases based on reverse transcription–polymerase chain reaction
- Patients should have a 12-lead electrocardiogram upon admission

Exclusion criteria

- Out-of-hospital mortality cases
- Pregnant women

The baseline characteristics were recorded on admission, including age, sex, body mass index, presenting vital signs, symptoms, comorbidities, medications, and laboratory findings.

The study adhered to the ethical considerations and principles set out in relevant guidelines, including the Declaration of Helsinki 2013, World Health Organization guidelines, International Conference on Harmonization—Good Clinical Practice, Data Privacy Act of 2012, and the National Ethics Guidelines for Health Research, and was approved by the Research Ethics Committee of the University of Santo Tomas Hospital (REC-2022-02-037-TF). Given the retrospective review of this study, informed consent was waived.

ECG Analysis

The criteria of parameter measurement and ECG diagnosis were based on the recommendation of the American Heart Association (American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society, 2007–2009).[21–26] The admission electrocardiogram was considered abnormal if at least one of the criteria for ECG abnormality was met:

- The definition of "any ECG abnormality" is as follows:
  - Sinus bradycardia in the absence of rate-lowering medications
  - Sinus tachycardia
  - Sinus arrhythmia
  - Presence of atrial fibrillation (AF), atrial flutter, atrioventricular (AV) nodal tachycardia, ventricular tachycardia, or ventricular fibrillation
  - Presence of atrial premature complexes or ventricular premature complexes
  - Presence of AV blocks (AVBs; first-, second-, or third-degree AVB)
  - Presence of right or left bundle-branch blocks or nonspecific interventricular conduction delay
  - Presence of chamber enlargements (left ventricular hypertrophy, right ventricular hypertrophy (RVH), left atrial abnormality, right atrial abnormality)
  - Presence of Brugada pattern
  - Presence of ST elevation, ST depression, or T-wave inversion
  - Presence of early repolarization pattern

All ECG analyses were derived from the first electrocardiogram recorded upon admission and were interpreted by two independent cardiologist readers to limit false-positive findings and interobserver variability. The cardiologists had no knowledge of any clinical data of the patient population including the outcome to eliminate bias.

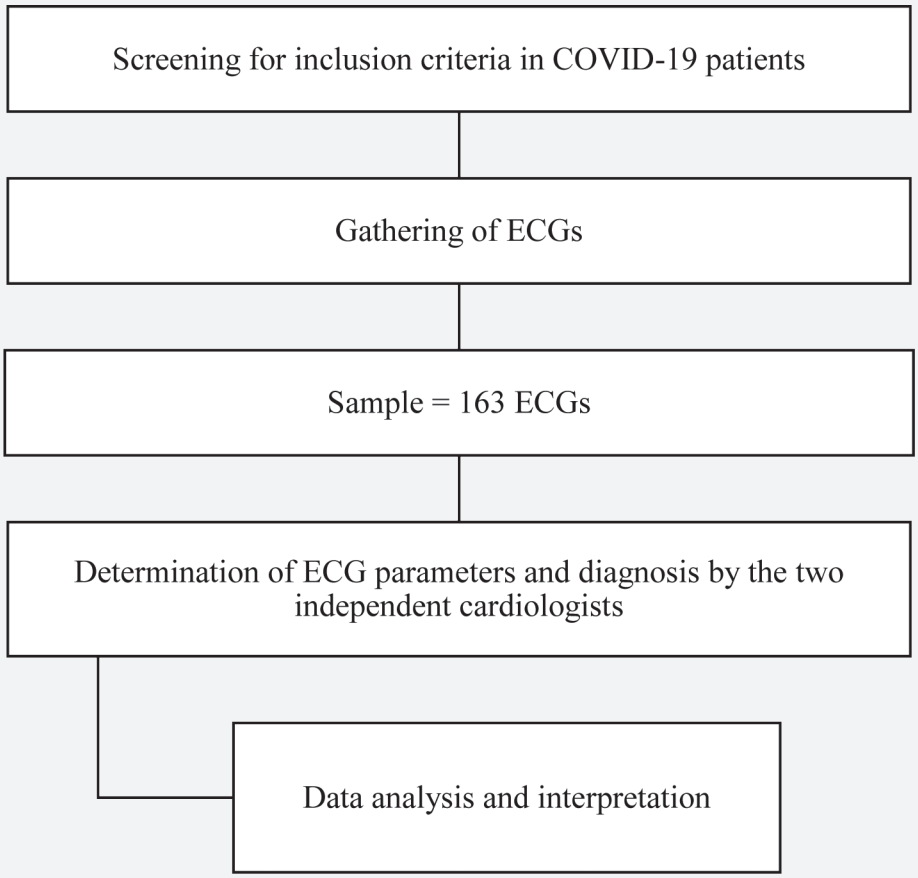

Figure 1. Flowchart of the study process. Abbreviations: COVID-19, coronavirus disease 2019; ECG, electrocardiogram.

Main Outcome

The primary outcome is a composite of all-cause in-hospital mortality.

Sample Size Calculation

A minimum of 152 COVID-19 patients were required for this study based on a level of significance of 5%, assuming 15%[12] of the patients will develop ECG abnormalities (Figure 1).

Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. Continuous variables were presented as mean (±SD) and compared using the *t* test or single-factor analysis of variance. Categorical variables were expressed as absolute values and proportions and compared using χ^2 or Fisher exact test. Univariate analysis for demographics, blood tests, and outcomes was performed between those with or without ECG abnormality and between nonsurvivors and survivors. $P < 0.05$ was considered significant. Statistical analyses were performed with JASP statistical software.

RESULTS

General Findings

A total of 163 hospitalized patients with COVID-19 infection met the inclusion criteria (Figure 2). The baseline demographic and clinical profiles of patients with COVID-19 based on the presence of any ECG abnormality and survival status are summarized in Tables 1 and 2, respectively.

The mean (±SD) age was 54.7 (±18.0) years; the median age was 55 years, and women represented 52.76% (n = 86) of the study population. There were 47 patients (28.83%) who had severe to critical COVID-19 infection, and 33 patients (20.25%) were admitted to the ICU. The mortality rate of this group of patients was 46.81% (22 patients). Overall, the mortality rate of COVID-19 patients during their hospitalization was 13.5% (22 of 163 patients). Patients who had any ECG abnormality and those who died were significantly older with a mean (±SD) age of 57.13 (±17.20) years and 71.65 (±9.44) years, respectively.

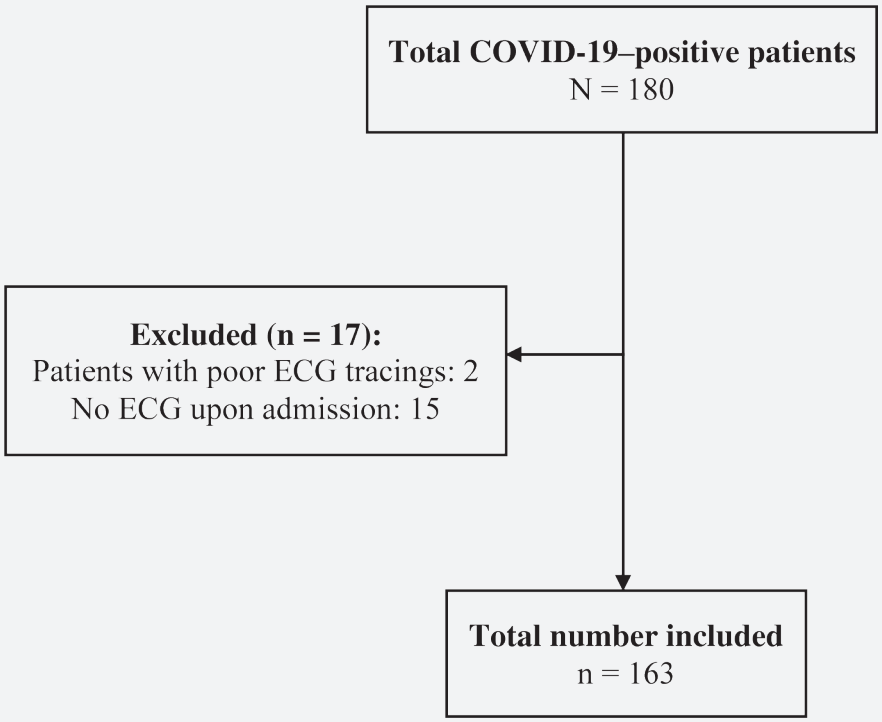

Figure 2. Flow pathway of patient inclusion.

About 79.75% (130) of the patients had CVDs. Hypertension (57.1%), diabetes mellitus (28.8%), prior stroke (10.4%), coronary artery disease (7.98%), and dyslipidemia (7.4%) were the most reported comorbidities (Tables 1 and 2).

As shown in Tables 1 and 2, both age and hypertension were significantly associated with the presence of any ECG abnormality and mortality. Other comorbidities that were significantly related to increased mortality risk in COVID-19 infection include dyslipidemia, coronary artery disease, and chronic heart failure. Likewise, laboratory parameters such as hemoglobin, ferritin, and estimated glomerular filtration rate were significantly associated with mortality.

ECG Findings

The presence of any ECG abnormality was detected in 78.5% (128) of COVID-19 patients, and it was significantly associated with in-hospital mortality ($P = 0.038$) (Table 3). That is, the survival status of COVID-19 patients does significantly depend on the ECG abnormalities for the given sample (n = 163). Notably, 95.45% (21 of 22) of the COVID-19 nonsurvivors presented with any ECG abnormality.

The ECG findings showed a variety of differences between survivors and nonsurvivors of COVID-19 infection (Table 4). The frequently detected ECG findings were sinus rhythm with any ECG abnormality (65%), nonspecific ST and T-wave changes (35%), and sinus tachycardia (22%). Other reported ECG findings, in decreasing order, include left ventricular hypertrophy (8.6%), abnormal precordial R-wave progression (7.4%), prolonged QTc (6.13%), old infarction (6%), AF or flutter (5%), and T-wave inversion (5%).

Increased mortality risk was significantly associated with ECG parameters such as ventricular rate, PR interval, and actual QT interval. Moreover, ECG findings of sinus rhythm with any ECG abnormalities ($P = 0.003$), AF or flutter ($P = 0.002$), supraventricular tachycardia ($P = 0.011$), ventricular tachycardia ($P = 0.011$), third-degree AVB ($P = 0.011$), T-wave inversion ($P = 0.005$), and RVH ($P = 0.011$) were also associated with in-hospital mortality (Table 4).

DISCUSSION

SARS-CoV-2, an enveloped, nonsegmented, single-stranded, positive-sense RNA virus is transmitted via respiratory droplets and aerosols from person to person. It binds to angiotensin-converting enzyme 2 in target cells such as lung alveolar epithelial cells and enterocytes of the small intestine. The virus-laden pneumocytes release various cytokines and inflammatory markers that lead to “cytokine storm,” thereby causing severe inflammation and lung injury. Patients may present with pneumonia, ARDS, multiorgan dysfunction, and hemodynamic instability, as well as several cardiovascular complications.[15]

Angiotensin-converting enzyme 2 is highly expressed in pericytes of adult human hearts, indicating intrinsic susceptibility of the heart to SARS-CoV-2 infection.[27] Dissemination of the COVID-19 virus may trigger a proinflammatory cascade

Table 1. Demographic and Clinical Profiles of COVID-19 Patients (n = 163) With ECG Abnormalities

Variables	Any ECG Abnormality (n = 128)	No ECG Abnormality (n = 35)	*P*
Age, mean ± SD, y	**57.13 ± 17.20**	**45.63 ± 18.62**	**0.001**[a]
Sex, n (%)			0.083
Male	65 (51)	12 (34)	
Female	63 (49)	23 (66)	
Obesity, n (%)	65 (51)	14 (40)	0.258
Smoking history, n (%)			
Never	83 (65)	27 (77)	0.383
Active smoker	10 (8)	2 (6)	
Former smoker	35 (27)	6 (17)	
Comorbidities, n (%)			
Hypertension	**82 (64)**	**11 (31)**	**0.001**[a]
Diabetes mellitus	38 (37)	9 (26)	0.646
Coronary artery disease	12 (9)	1 (3)	0.207
Chronic heart failure	9 (7)	0 (0)	0.107
COPD	4 (3)	0 (0)	0.290
Prior stroke	15 (12)	2 (6)	0.303
Active cancer	7 (5)	2 (6)	0.955
Permanent pacing	3 (2)	0 (0)	0.361
Presenting vital signs, mean ± SD			
Heart rate, beats/min	91.04 ± 14.57	87.80 ± 13.35	0.237
Respiratory rate, breaths/min	21.82 ± 3.06	20.74 ± 2.01	0.051
Systolic blood pressure, mm Hg	126.30 ± 15.16	121.43 ± 17.68	0.106
Diastolic blood pressure, mm Hg	76.92 ± 8.43	75.43 ± 10.39	0.379
Oxygen saturation, %	94.72 ± 6.95	93.31 ± 16.52	0.623
Laboratory findings, mean ± SD			
Hemoglobin, g/L	133.98 ± 17.99	132.83 ± 16.81	0.733
HsTrop I, ng/L	1.21 ± 13.08	0.02 ± 0.09	0.591
d-Dimer, ng/mL	3.0 ± 13.36	0.70 ± 1.30	0.313
Ferritin, µg/L	1323.93 ± 1767.37	1436.35 ± 4121.85	0.811
LDH, U/L	410.08 ± 1177.31	237.63 ± 172.58	0.390
eGFR	82.65 ± 31.89	89.78 ± 38.43	0.203
ECG parameters, mean ± SD			
Atrial rate	88.73 ± 33.51	83.97 ± 12.07	0.188
Ventricular rate	**92.31 ± 24.49**	**83.97 ± 12.07**	**0.006**[a]
PR interval, ms	**0.16 ± 0.06**	**0.17 ± 0.02**	**0.045**[a]
QRS complex	0.08 ± 0.02	0.08 ± 0.01	0.055
QT interval, ms	0.35 ± 0.06	0.35 ± 0.03	0.358
QTc-Bazette	0.42 ± 0.06	0.42 ± 0.03	0.949
QTc-Fridericia	0.40 ± 0.06	0.40 ± 0.22	0.823

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HsTrop I, high-sensitivity troponin-I; LDH, lactate dehydrogenase.

[a] *Significant at the 0.05 level.*

Table 2. Demographic and Clinical Profiles of COVID-19 Patients (n = 163) Based on Their Survival Status

Variables	Survivors (n = 141)	Nonsurvivors (n = 22)	*P*
Age, mean ± SD	52.13 ± 17.82	70.82 ± 9.53	**0.000**[a]
Sex			0.231
Male	64 (45)	13 (59)	
Female	77 (55)	9 (41)	
Obesity	72 (50)	7 (35)	0.093
Smoking history			
Never	100 (71)	10 (45)	**0.002**[a]
Active smoker	12 (9)	0	
Former smoker	29 (20)	12 (55)	
Comorbidities, n (%)			
Hypertension	73 (51)	20 (100)	**0.001**[a]
Diabetes mellitus	38 (27)	9 (45)	0.179
CAD	8 (6)	5 (25)	**0.006**[a]
Chronic heart failure	5 (3)	4 (20)	**0.005**[a]
COPD	4 (3)	0	0.424
Prior stroke	13 (9)	4 (20)	0.201
Active cancer	7 (5)	2 (10	0.431
Permanent pacing	2 (1)	1 (5)	0.310
Dyslipidemia	8 (6)	4 (25)	**0.037**[a]
Presenting vital signs, mean ± SD			
Heart rate, beats/min	89.65 ± 13.65	94.82 ± 17.89	0.116
Respiratory rate, breaths/min	21.09 ± 2.20	24.82 ± 4.43	**0.001**[a]
Systolic blood pressure, mm Hg	125.11 ± 15.79	126.23 ± 16.21	0.758
Diastolic blood pressure, mm Hg	76.38 ± 8.89	78.00 ± 8.86	0.428
Oxygen saturation, %	94.83 ± 10.21	91.80 ± 5.74	0.178
Laboratory findings, mean ± SD			
Hemoglobin, g/L	134.98 ± 17.54	125.77 ± 17.00	**0.026**[a]
HsTrop I, ng/L	1.07 ± 12.46	0.22 ± 0.64	0.752
d-Dimer, ng/mL	0.87 ± 1.39	12.99 ± 30.70	0.078
Ferritin, µg/L	989.43 ± 1230.87	3691.63 ± 5448.66	**0.031**[a]
LDH, U/L	351.48 ± 1117.91	511.27 ± 339.01	0.508
eGFR	87.34 ± 31.96	58.16 ± 32.34	**0.000**[a]

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HsTrop I, high-sensitivity troponin-I; LDH, lactate dehydrogenase.
[a] Significant at the 0.05 level.

in the cardiovascular system, leading to myocarditis, loss of contractile function, altered ejection fraction, damage to cardiomyocytes, and release of cardiac injury markers, such as cardiac troponin T and brain natriuretic peptide into the blood. The endothelium was also found to have high expression of angiotensin-converting enzyme 2 receptors causing endothelial damage and vasoconstriction, which may lead to ischemia, vascular inflammation, and thrombosis.[28] COVID-19 infection can also lead to cardiac rhythm abnormalities from increased sympathetic nervous system activity due to myocarditis and proinflammatory state. Other contributing factors that may lead to developing or aggravating arrhythmic complications include hypoxic injury, hypotension, electrolyte abnormalities, plaque rupture, coronary spasm, and direct myocardial injury.[29]

In this retrospective observational study of patients with COVID-19 infection, we obtained the following key findings: (1) any ECG abnormality at admission is common and related to

Table 3. Association of ECG Abnormalities of COVID-19 Patients (n = 163) and In-hospital Mortality

Group	Any ECG Abnormality	No ECG Abnormality	*P*
Dead	107	34	**0.038**[a]
Alive	21	1	

Abbreviations: COVID-19, coronavirus disease 2019; ECG, electrocardiogram.
[a] *Significant at the 0.05 level.*

in-hospital mortality, and (2) cardiac dysrhythmias such as AF or flutter, supraventricular tachycardia, ventricular tachycardia, and third-degree AVB were among the ECG abnormalities associated with in-hospital mortality.

In this study, only 21.5% of patients presented with normal sinus rhythm with no concomitant ECG abnormality, a finding similar to the study by Li et al.[18] Majority of the patients had ECG findings of sinus rhythm with any ECG abnormality (65%), nonspecific ST and T-wave changes (35%), and sinus tachycardia (22%), which were also reported in several studies.[12,15–18,30] However, a study by Ozaeta et al[31] on the ECG findings of COVID-19 in the Philippines revealed other commonly reported ECG abnormalities such as prolonged QT, ischemia, and fascicular blocks. The same study also reported that most of the mortality (90.1%) had ECG abnormalities, a finding consistent with the result of our study, where 95.5% of the patients who died of COVID-19 presented with any ECG abnormalities on admission. These include sinus tachycardia, supraventricular tachycardia, ventricular tachycardia, third-degree AVB, nonspecific ST and T-wave changes, old infarction, and RVH.

Most frequently, sinus tachycardia was seen in patients with COVID-19. Cho et al reported in their prospective study that sinus tachycardia serves as a significant prognostic factor and is associated with an increased risk of death.[30] Its causes are multifactorial such as fever, dyspnea, hypoxia, shock, anxiety, and inflammatory response against SARS-CoV-2.[27,32] These causes may also result in nonspecific ST–T-wave changes, which is also not an uncommon ECG finding in patients with COVID-19. Notably, it was found in a recent study that sinus tachycardia and nonspecific ST and T-wave changes were the frequently reported ECG findings of pulmonary embolism in COVID-19 patients. The classic S1Q3T3 pattern were seen in only less than 10% of the patients.[33]

Malignant arrhythmias including ventricular tachycardia and third-degree AVB were seen in only 0.6% of patients, respectively. Although rare, our study showed that these arrhythmias significantly portend mortality risk. Similar results were found in a study by Cho et al, where sustained ventricular tachycardia and ventricular fibrillation occurred in 1.4% and 0.7% of patients, respectively. Other studies in China reported a higher incidence of malignant arrhythmias from 5.9% to 16.7%.[19,34] This discrepancy may be due to the different admission criteria between centers. Our institution admits mild to critical COVID illness, whereas admissions in China were mostly patients with severe COVID-19 cases.[34] These fatal arrhythmias may result from myocarditis causing direct invasion into the heart and cytokine storm.[19] It may also be attributed to metabolic disorders, hypoxia, or neurohormonal imbalance in patients with or without underlying CVD.[32]

In our study, AF occurred in 6.13% of patients, which is consistent with other cohort studies.[18,20,35,36] In other studies, 9% to 12% of patients had a high prevalence of AF.[12,30] Critically ill COVID-19 patients and those needing intensive care had a much higher incidence of AF at 22% and up to 50%, respectively.[34,37] A probable explanation of AF in COVID-19 is pulmonary hypertension as a consequence of ARDS. It results to increased right atrial pressure and atrial stretch and electrical or structural changes in cardiac myocytes as a response to increased atrial tissue matrix stiffness, thus creating a substrate for AF.[38,39]

Another significant finding in our study is the correlation of RVH with mortality risk. Right ventricular hypertrophy occurred in 5% of patients who died of COVID-19. Studies showed that ECG criteria for RVH are neither sensitive nor specific for the screening of mild RVH in adults without underlying CVD.[40] However, in patients with ARDS, RVH and right ventricular failure are common and are predictors of mortality.[41] In a case series on the ECG findings of acute RVH in COVID-19 pneumonia by Martínez-Mateo et al,[42] the presence of ECG signs for RVH was a predictor of right ventricular dilatation in transthoracic echocardiography and a hallmark of the severity of COVID-19 pneumonia. The most common sign is the S_IQ_{III} pattern, which may also be found in patients with massive pulmonary embolism. Therefore, RVH may be secondary to pulmonary vasoconstriction and acute lung injury in ARDS or pulmonary embolism because of the exaggerated inflammatory state and thrombosis in COVID-19.[42]

Interestingly, the study showed a significant association between PR and QT intervals and mortality. Pavri et al[43] studied in a cohort cross-sectional analysis the PR interval behavior in patients with COVID-19 by evaluating the relationship of PR interval to heart rate (PR:HR) slope with mortality and need for endotracheal intubation. Normally, the PR interval shortens as HR increases, a physiological adaptation that preserves AV synchrony, and maintains adequate ventricular filling during HR acceleration. However, it has been shown that in patients with COVID-19 the PR interval showed prolongation or absence of shortening with increasing HR in 49.3% of patients. This PR interval behavior was associated with both a higher risk of mortality and the need for endotracheal intubation. The underlying pathophysiology remains unknown, but a proposed

Table 4. ECG Parameters and Abnormalities of COVID-19 Patients (n = 163) Based on Their Survival Status

Variables	Survivors (n = 141)	Nonsurvivors (n = 22)	*P*
ECG parameters, mean ± SD			
Atrial rate	85.52 ± 20.65	101.68 ± 63.08	0.246
Ventricular rate	**87.09 ± 16.54**	**112.55 ± 39.26**	**0.007**
PR interval, ms	**0.17 ± 0.04**	**0.11 ± 0.08**	**0.003**[a]
QRS complex	0.08 ± 0.19	0.09 ± 0.03	0.207
Actual QT interval, ms	**0.36 ± 0.04**	**0.30 ± 0.11**	**0.038**[a]
QTc-Bazette	0.42 ± 0.04	0.39 ± 0.13	0.234
QTc-Fridericia	0.40 ± 0.03	0.37 ± 0.13	0.247
ECG findings, n (%)			
Sinus rhythm (with other ECG abnormalities)	97 (69)	8 (36)	**0.003**[a]
Sinus bradycardia	4 (3)	0	0.424
Sinus tachycardia	28 (20)	7 (32)	0.204
Sinus arrhythmia	6 (4)	1 (5)	0.950
Ectopic atrial rhythm	2 (1.4)	0	0.574
Atrial fibrillation or flutter	**4 (3)**	**4 (18)**	**0.002**[a]
Supraventricular tachycardia	**0**	**1 (5)**	**0.011**[a]
Ventricular tachycardia	**0**	**1 (5)**	**0.011**[a]
APCs	7 (5)	1 (5)	0.933
VPCs	5 (4)	1 (5)	0.817
First-degree AV block	4 (3)	1 (5)	0.666
Third-degree AV block	**0**	**1 (5)**	**0.011**[a]
Fragmented QRS	5 (4)	0	0.370
RBBB	4 (3)	2 (9)	0.147
LBBB	0	0	NA
Left anterior fascicular block	1 (0.7)	0	0.692
Abnormal precordial R-wave progression	10 (7)	2 (9)	0.738
Brugada pattern	3 (2)	0	0.490
Acute ST elevation	1 (0.7)	0	0.692
T-wave inversion	**5 (4)**	**4 (18)**	**0.005**[a]
Old infarction	7 (5)	3 (14)	0.115
Nonspecific ST and T-wave changes	52 (37)	5 (23)	0.195
RVH	**0**	**1 (5)**	**0.011**[a]
LVH	12 (9)	2 (9)	0.928
Left atrial abnormality	3 (2)	0	0.490
Early repolarization pattern	2 (1.4)	0	0.574
Prominent U waves	4 (3)	0	0.424
Prolonged QTc	7 (5)	3 (14)	0.115
Low-voltage limb leads	4 (3)	0	0.424

Abbreviations: APCs, atrial premature complexes; AV, atrioventricular; COVID-19, coronavirus disease 2019; ECG, electrocardiogram; I LBBB, left bundle branch block; LVH, left ventricular hypertrophy; RBBB, right bundle-branch block; RVH, right ventricular hypertrophy; VPCs, ventricular premature complexes.

[a] *Significant at the 0.05 level.*

underlying mechanism is the role of elevated anticardiolipin antibodies and activated thromboplastin time in patients with COVID-19, thereby causing antigen-antibody reaction affecting the cardiac conduction system.[43]

In several studies, QT interval prolongation has been found to occur frequently in 26% to 39% of COVID-19 patients.[12,31,35,37] Antiviral and antimalarial drugs used for treating COVID-19 were considered as the main cause.[18] Sacher et al confirmed that hydroxychloroquine, lopinavir/ritonavir, and azithromycin prolong the QTc interval in patients with COVID-19.[18,44] In our study, however, it revealed a relatively low incidence of prolonged QT at 6.13%. Such a result may be because all electrocardiograms were taken upon hospital admission, that is, prior to the initiation of any drugs used for treating COVID-19. Furthermore, other contributory factors to prolonged QT include electrolyte imbalances and inflammatory markers such as tumor necrosis factor α and interleukin 6.[45]

Notably, three patients presented with the Brugada pattern. COVID-19 infection may unmask a Brugada pattern and serves as a risk factor for developing proarrhythmic complications due to virus-related issues such as fever, electrolyte disturbance, and inflammatory stress brought along with COVID-19 infection. Uncontrolled fever has been shown to precipitate arrhythmia and sudden cardiac death in patients with Brugada syndrome.[46] Cardiac sodium (Na^+) channels are inactivated at higher temperatures. The decreased Na^+ flow can result in the shortening of the intrapericardial dispersion of the action potential duration, thereby facilitating phase 2 reentry ventricular arrhythmias and sudden death.[47] It is therefore recommended to initiate aggressive antipyretic therapy in COVID-19 patients with Brugada pattern.

CONCLUSION

Cardiovascular involvement in patients with COVID-19 infection may result in ECG abnormalities, which are significantly associated with increased risk for in-hospital mortality. These ECG abnormalities include AF or atrial flutter, supraventricular tachycardia, ventricular tachycardia, third-degree AVB, T-wave inversion, and RVH. Other novel findings in this study are cardiovascular comorbidities, and increased age was not uncommon in patients with COVID-19 infection and was also significantly associated with increased mortality risk. More importantly, a standard 12-lead electrocardiogram on admission can help clinicians promptly assess cardiac complications and stratify patients at increased risk of death for COVID-19, which may warrant closer monitoring.

LIMITATIONS OF THE STUDY

The following limitations of our study must be acknowledged. First, electrocardiograms included in this study were those taken upon admission only. Previous and/or repeat electrocardiograms of the patients were not accounted for; thus, new-onset, chronic, and/or transient ECG abnormalities could not be distinguished. Second, cardiac involvement, whether from an underlying cardiac illness or a complication of the COVID-19 infection, could not be accurately established because electrocardiograms done upon admission were only assessed. Finally, this study had no detailed data on the various pharmacologic interventions given to the patients; hence, the effect of the treatments on the ECG findings and its influence on in-hospital mortality could not be established.

RECOMMENDATIONS

A similar retrospective or prospective study taking into consideration the patient's prior and/or repeat electrocardiograms is recommended to achieve a more accurate conclusion on the weight of the ECG abnormalities and its association with in-hospital mortality. A more comprehensive study including data on patient treatments and correlation with echocardiographic findings is recommended to better delineate the underlying cause of the ECG abnormality.

ACKNOWLEDGMENT

The authors extend their gratitude to the Section of Adult Cardiology of the University of Santo Tomas Hospital for their constant guidance and support.

CONFLICT OF INTEREST

The contributing authors declare no conflict of interest related to this research.

FUNDING/SUPPORT

The authors received no funding or financial support for this research.

DECLARATIONS

- **Approval of the research protocol:** The study adhered to the ethical considerations and principles set out in relevant guidelines, including the Declaration of Helsinki 2013 and World Health Organization guidelines, and was approved by the Research Ethics Committee of the University of Santo Tomas Hospital (REC-2022-02-037-TF).
- **Informed consent:** Given the retrospective review of this study, informed consent was waived.

REFERENCES

1. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

2. Republic of the Philippines Department of Health. COVID-19 case tracker. https://doh.gov.ph/2019-ncov.
3. Hui KPY, Cheung M-C, Perera RA, et al. Tropism, replication competence, and innate immune response of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures. *Lancet Respir Med* 2020;8:687–695.
4. Wiersinga W, Rhodes A, Cheng A, et al. Pathophysioloogy, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19). A review. *JAMA* 2020;324(8):782–793.
5. Parasher A. COVID-19: current understanding of its pathophysiology, clinical presentation and treatment. *Postgrad Med J* 2021;97:312–320.
6. Macedo A, Goncalves N, Febra C. COVID-19 fatality rates in hospitalized patients: systematic review and meta-analysis. *Ann Epidemiol* 2021;57:14–21.
7. Oliveira E, Parik A, Lopez-Ruiz A, et al. ICU outcomes and survival in patients with severe COVID-19 in the largest health care system in central Florida. *PLoS One* 2021;16(3):e0249038.
8. Salamat M, Malundo A, Abad C, et al. Characteristics and factors associated with mortality of 200 COVID-19 patients at a Philippine COVID-19 tertiary referral center. *Acta Med Philipp* 2021;55:173–182.
9. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol* 2020;109(5):531–538.
10. Abraha H, Gessesse Z, Gebrecherkos T, et al. Clinical features and risk factors associated with morbidity and mortality among patients with COVID-19 in northern Ethiopia. *Int J Infect Dis* 2021;105:776–783.
11. Lee KH, Kim JS, Hong SH, et al. Risk factors of COVID-19 mortality: a systematic review of current literature and lessons from recent retracted articles. *Eur Rev Med Pharmacol Sci* 2020;24:13089–13097.
12. Pishgahi M, Yousefifard M, Safari S, Ghorbanpouryami F. Electrocardiographic findings of COVID-19 patients and their correlation with outcome: a prospective study. *Adv J Emerg Med* 2021;5(2):Spring (April).
13. Ranard L, Fried J, Abdalla M, et al. Approach to acute cardiovascular complications in COVID-19 infection. *Circ Heart Fail* 2020;13:167–176.
14. Iqubal A, Kashif Iqubal M, Hoda F, et al. COVID-19 and cardiovascular complications: an update from the underlying mechanism to consequences and possible clinical intervention. *Expert Rev Anti Infect Ther* 2021;19(9):1083–1092. doi:10.1080/14787210.2021.1893692.
15. Long B, Brady W, Koyfman A, et al. Cardiovascular complications in COVID-19. *Am J Emerg Med* 2020:38:1504–1507.
16. Lee C, Ali K, Connell D, et al. COVID-19 associated cardiovascular complications. *Diseases* 2021;9:47.
17. Li L, Zhang S, He B, et al. Risk factors and electrocardiogram characteristics for mortality in critical inpatients with COVID-19. *Clin Cardiol* 2020;43:1624–1630.
18. Li Y, Liu T, Tse G, et al. Electrocardiographic characteristics in patients with coronavirus infection: a single-center observational study. *Ann Noninvasive Electrocardiol* 2020;25:e12805.
19. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;5(7):811–818.
20. de Vita A, Ravenna S, Covino M, et al. Electrocardiographic findings and clinical outcome in patients with COVID-19 or other acute infectious respiratory diseases. *J Clin Med* 2020;9:3647.
21. Mason JW, Hancock EW, Gettes LS. Recommendations for the standardization and interpretation of the electrocardiogram: part II: electrocardiography diagnostic statement list. A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2007;49:1128–1135.
22. Mason JW, Hancock EW, Gettes LS. Recommendations for the standardization and interpretation of the electrocardiogram: part II: electrocardiography diagnostic statement list. *Circulation* 2007; 115(10). https://doi.org/10.1161/CIRCULATIONAHA.106.180201
23. Surawicz B, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances. *J Am Coll Cardiol* 2009;53: 976–981.
24. Rautaharju PM, Surawicz B, Gettes LS. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part IV: the ST segment, T and U waves, and the QT interval. *J Am Coll Cardiol* 2009;53: 982–991.
25. Hancock EW, Deal BJ, Mirvis DM, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy. *J Am Coll Cardiol* 2009;53:992–1002.
26. Wagner GS, Macfarlane P, Wellens H, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction. *J Am Coll Cardiol* 2009;53:1003–1011.
27. Chen L, Li X, Chen M, et al. The ACE2 expression l human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. *Cardiovasc Res* 2020;116(12):1994.
28. Iqubal A, Iqubal MK, Hoda F, Najmi AK, Haque SE. COVID-19 and cardiovascular complications: an update from the underlying mechanism to consequences and possible clinical intervention. *Expert Rev Anti Infect Ther* 2021;19(9):1083–1092.
29. Kochi A, Tagliari AP, Forleo, G, et al. Cardiac and arrhythmic complications in patients with COVID-19. *J Cardiovasc Electrophysiol* 2020;31:1003–1008.

30. Cho JH, Namazi A, Shelton R, et al. Cardiac arrhythmias in hospitalized patients with COVID-19: a prospective observational study in the western United States. *PLoS One* 2020;15(12).
31. Ozaeta MK, dela Cruz FD, Sombrero MC, et al. Electrocardiogram and echocardiographic findings of COVID-19 in Makati Medical Center. *ASEAN Heart J* 2020;29:1–7.
32. Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. *J Am Coll Cardiol* 2020;75(18):2352–2371.
33. Kho J, Ioannou A, van den Abbeele K, Mandal AKJ, Missouris CG. Pulmonary embolism in COVID-19: clinical characteristics and cardiac implications. *Am J Emerg Med* 2020;38(10):2142–2146.
34. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA* 2020;323(11):1061–1069.
35. Denegri A, Pezzuto G, D'Arienzo M, et al. Clinical and electrocardiographic characteristics at admission of COVID-19/SARS-CoV2 pneumonia infection. *Intern Emerg Med* 2021;16(6):1451–1456.
36. Yuan M, Zathar Z, Nihaj F, et al. ECG changes in hospitalised patients with COVID-19 infection. *Br J Cardiol* 2021;28(2):24.
37. Bertini M, Ferrari R, Guardigli G, et al. Electrocardiographic features of 431 consecutive, critically ill COVID-19 patients: an insight into the mechanisms of cardiac involvement. *Europace* 2020;22(12):1848–1854.
38. Stone E, Kiat H, McLachlan C. Atrial fibrillation in COVID-19: a review of possible mechanisms. *Fed Am Soc Exp Biol* 2020;34:11347–11354.
39. Wanamaker B, Cascino T, McLaughlin V, Oral H, Latchamsetty R, Siontis KC. Atrial arrhythmias in pulmonary hypertension: pathogenesis, prognosis and management. *Arrhythm Electrophysiol Rev* 2018;7(1):43–48.
40. Whitman I, Patel V, Soliman E, Bluemke D, Praestgaard A, Jain A. Validity of the surface electrocardiogram criteria for right ventricular hypertrophy: the MESA—right ventricle study. *J Am Coll Cardiol* 2014;63:672–681.
41. Repessé X, Charron C, Viellard-Baron A. Right ventricular failure in acute lung injury and acute respiratory distress syndrome. *Minerva Anestesiol* 2012;78:941–948.
42. Martínez-Mateo V, Fernández-Anguita MJ, Paule A. Electrocardiographic signs of acute right ventricular hypertrophy in patients with COVID-19 pneumonia: a clinical case series. *J Electrocardiol* 2020;62:100–102.
43. Pavri B, Kloo J, Farzad D, Riley J. Behavior of the PR interval with increasing heart rate in patients with COVID-19. *Heart Rhythm* 2020;17(9):1434–1438.
44. Sacher F, Fauchier L, Boveda S, et al, Working Group of Pacing, Electrophysiology of the French Society of Cardiology, the Board of the French Society of Cardiology. Use of drugs with potential cardiac effect in the setting of SARS-CoV-2 infection. *Arch Cardiovasc Dis* 2020;113(5):293–296.
45. Cipriani A, Zorzi A, Ceccato D, et al. Arrhythmic profile and 24-hour QT interval variability in COVID-19 patients treated with hydroxychloroquine and azithromycin. *Int J Cardiol* 2020;316:280–284.
46. Roterberg G, El-Battrawy I, Veith M, et al. Arrhythmic events in Brugada syndrome patients induced by fever. *Ann Noninvasive Electrocardiol* 2019;25:e12723.
47. Zimmermann P, Aberer F, Braun M, Sourij H, Moser O. The arrhythmogenic face of COVID-19: Brugada ECG pattern in SARS-CoV-2 infection. *J Cardiovasc Dev Dis* 2022;9(4):96.