Electrocardiographic Abnormalities predicting mortality in COVID-19 pneumonia patients

Nidhi Kaeley¹, Prakash Mahala¹, Rohit Walia²

¹Department of Emergency Medicine, All India Institute of Medical Science, Rishikesh, Uttarakhand, ²Department of Cardiology, All India Institute of Medical Science, Bathinda, Punjab, India

ABSTRACT

Background: Cardiovascular involvement is a significant cause of death in COVID pneumonia. Early electrocardiographic changes may predict cardiovascular involvement and predict mortality in COVID pneumonia patients. Methods: A total of 250 consecutive patients with COVID-19 pneumonia admitted to the emergency were studied for electrocardiographic abnormalities and their relation to mortality. Results: Most patients required supplemental oxygen to maintain optimal saturation. A total of 72% showed ECG abnormalities, and the overall cohort had a mortality of 50%. New-onset atrial fibrillation, left bundle branch block or right bundle branch pattern, and ventricular premature complexes were associated with high mortality. Sinus tachycardia and atrial fibrillation were the most common arrhythmia and were significantly associated with mortality. Conclusions: New-onset atrial fibrillation, intraventricular conduction defects, and sinus tachycardia are associated with increased mortality in COVID pneumonia patients.

Keywords: Atrial fibrillation, COVID-19, electrocardiogram, intraventricular conduction defects, SARS-CoV-2

Introduction

COVID-19 can be associated with myocarditis, decompensated heart failure, acute coronary syndrome, and arrhythmias.¹⁻⁴ Electrocardiogram (ECG) is the simplest and readily available method to screen for the possible presence of cardiac abnormalities. It is easy to read and can be utilized by primary physicians for risk assessment. In this study, we explored ECG abnormalities in COVID-19 pneumonia patients which may predict mortality and poor outcome.

Materials and Methods

We studied consecutive patients admitted to the Emergency Department of our University teaching tertiary care hospital with the diagnosis of COVID-19 pneumonia during the period from August 1, 2020, to January 15, 2021. Out of 350 COVID-19 pneumonia patients admitted, 250 had ECG records and were included. Patients with old myocardial infarction, electrolyte abnormalities, and antiarrhythmic drugs were excluded [Figure 1]. The study was approved by the ethics committee of our institution, registered in the clinical trial registry of India, was conducted as per the latest guidelines of the declaration of Helsinki and written, and whenever not possible telephonic verbal informed consent was taken from participants or relatives.

Aims and Objectives

In this study, we aimed to evaluate different rates of ECG abnormalities and assess the prognostic implications of ECG changes in patients who recovered and were discharged successfully vs. those who died during the hospital stay.

Inclusion and exclusion criteria

COVID-19 pneumonia was diagnosed using reverse-transcription polymerase chain reaction (RT-PCR) for severe acute respiratory
syndrome coronavirus-2 (SARS-CoV-2) on nasopharyngeal swabs. Chest X-ray and computerized tomography (CT) scan of the chest were performed. The demographic characteristics and clinical and laboratory data on admission were acquired from our institutional database. ECG was done at the baseline and during the course of hospitalization as indicated. Cardiac biomarkers and inflammatory markers were done as clinically indicated. The institutional ethics committee approved the study. Clinical improvement was defined as the resolution of fever for ≥48 h and the suspension of oxygen supplementation. Treatment as per the Indian council of medical research (ICMR) and hospital protocol was given to all patients. Patients with an old history of coronary artery disease or old myocardial infarction (2.8%, ten patients out of 350 patients), those already on antiarrhythmic drugs (1.42%, five patients out of 350 patients), or with abnormal serum K⁺ (0.57%, 2 out of 350 patients) were excluded from the analysis [Figure 1: Study Flow Diagram].

Routine hematological testing, including hemoglobin (Hb) concentration, white blood cell (WBC), platelets (PLT), neutrophil and lymphocytes counts, serum glucose, urea, creatinine, sodium, potassium, chloride, liver and renal function tests, albumin, ferritin, CRP and high-sensitive cardiac troponin I was done.

**Electrocardiography**

ECG was recorded with 25 mm/s, 1 mV/cm calibration, and 0.05–150 Hz filter setting. The ECGs were analyzed for the following parameters: rhythm, atrioventricular blocks, intraventricular conduction defects, ST-segment, T-wave abnormalities, and arrhythmias were recorded. Patients with left bundle branch block (LBBB) were excluded from ST-segment and T wave analyses, whereas in patients with right bundle branch block (RBBB), only leads V1–V4 were excluded from ST-segment and T wave analysis. ST-segment depression (STD) was diagnosed when a horizontal or downsloping displacement of the ST segment below the isoelectric line ≥0.5 mm, persisting at 0.08 s from the J point was detectable in at least two contiguous leads. ST-segment elevation (STE) was diagnosed when the J point was elevated by ≥1 mm, and morphology was judged to be compatible with an ischemic or pericarditis origin. An abnormal T-wave was diagnosed in the case of T-wave inversion ≥1 mm in at least two contiguous leads (except V1 and aVR). PR interval was measured from the beginning of the P-wave and the end of the R wave, and QRS interval was measured from the beginning of the Q-wave to the end of the S wave. The QT interval was defined as the interval from the onset of the QRS complex to the end of the T wave. Measurements of QT interval were performed from all leads, and the longest QT interval was recorded. The R-R interval was measured and used to compute the heart rate. Correct QT interval (QTc) was calculated using Bazett’s formula: QTc = QT/R-R interval. ECG analysis data of the patients were performed by two cardiologists.

**Clinical outcome**

We divided the patients into two groups those who had in-hospital mortality and those who were successfully discharged for analysis.

**Statistical analysis**

The data were reported as mean and standard deviation for continuous variables and number and proportions for discrete variables. We present data as mean ± standard deviation (SD) for continuous variables and proportions for categorical variables. Mean values of variables were compared by paired or independent sample t-test. In 2-tailed tests, P values < 0.05 were considered statistically significant.

**Results**

**Baseline characteristics**

The mean age was 55.94 ± 15.84 years with 86.0% males, 17.6% were hypertensive, and 20.8% were diabetics. The majority were sick patients requiring supplanted oxygen to maintain optical oxygen saturation. ECG abnormalities were present in 72% of the patients. Remdesvir was given in around 45% of the patients and Tocilizumab in 1.6%, and Favirapin in 2.8% of the patients [Table 1]. The patients were triaged in an emergency and then admitted to the emergency ward or intensive care unit, depending on clinical condition and need for mechanical ventilation.

**Total COVID cases ECG features**

Sinus tachycardia and atrial fibrillation were the most common arrhythmia. Both were associated with high mortality.
Intraventricular conduction defects, right bundle branch block more commonly than left bundle branch block were associated with high mortality [Table 2]. Ventricular premature complexes were associated in a small percentage of patients but were associated with mortality. Other parameters like ST-T changes and QT prolongation were not significant.

Discussion

Our COVID cohort included high-risk patients with > 90% requiring oxygen supplementation to maintain optimal saturation at admission to the emergency department. Nineteen percent of the patients required noninvasive or mechanical ventilation at presentation to the emergency department. Another major cause of mortality was extensive COVID pneumonia, adult respiratory distress syndrome, multiorgan dysfunction, sepsis, and renal insufficiency. This cohort has a mortality of approximately 50%.

Arrhythmias in COVID-19

Atrial fibrillation (AF) was the most common serious arrhythmia. All patients were on supplemental oxygen support. Two patients had high IL 6, AF occurred with normal serum potassium (K⁺) levels. Death was seen in all AF patients. Metabolic derangements, hypoxia, acidosis, intravascular volume imbalances, neurohormonal and autonomic imbalance, and catecholaminergic stress have been implicated in the causation of arrhythmias in COVID-19 patients. It is an common sequel of critical illness, with an estimated prevalence of almost 10% in ICU patients and predicts adverse outcomes. Sinus rhythm restoration is of high priority as it improves the patient’s hemodynamics. AF may attenuate cardiac output due to impaired left ventricular filling, especially with a rapid ventricular response. It has been reported that about 27.5% of COVID-19 patients admitted to the ICU developed an atrial tachyarrhythmia (of which 63% had AF). Altered IL-6 functional expression is also a common feature of supraventricular arrhythmias, including AF, leading to higher risks of death and cardiovascular events in AF patients. Cytokine storm, inflammation, and raised IL-6 and other cytokines have been associated with atrial fibrillation (AF), heart failure, coronary artery disease, torsade de pointes (TDP), and QT prolongation were not significant.

Sinus tachycardia: Most common ECG abnormality

Additionally, severe infection induces the sympathetic nervous system (SNS), and there is also a relationship between SNS activity and supraventricular tachyarrhythmia. Tachycardia is an independent prognosticator or mortality in patients with sepsis. Postulated mechanisms of this arrhythmogenesis include SNS-induced calcium entry into cardiac myocytes and a spontaneous release of calcium from the sarcoplasmic reticulum.

Intraventricular conduction defects

RBBB and LBBB were associated with high mortality. RBBB might be due to right ventricular involvement secondary to lung disease, right ventricular pressure overload, and pulmonary embolism. The patients developing RBBB were oxygen-dependent and had high CT scores for lung involvement. Undiagnosed cardiac involvement or conduction system involvement and rapid deterioration is also a possibility at the later course of the disease.
McCullough et al. also noted a higher incidence of death with RBBBand left-sided intraventricular conduction defects in patients with COVID-19 pneumonia. RBBB may reflect a higher incidence of right ventricular dysfunction in this group secondarily to extensive pulmonary involvement.\textsuperscript{24} Ying Wang et al. also noted sinus tachycardia and atrial fibrillation as independent risk factors for mortality.\textsuperscript{25} Sinus tachycardia can be due to fever, hypovolemia, heart failure, hypoxia, myocardial injury. Brit Long et al.\textsuperscript{26} also found sinus tachycardia as most common arrhythmia followed by atrial fibrillation and less commonly ventricular and bradyarrhythmia in their case series.

**Limitations**

Cardiac biomarkers, serum IL 6, and echocardiography were not performed in all patients.

**Conclusions**

Electrocardiographic abnormalities were found in most of the COVID-19 pneumonia patients requiring hospitalization. New-onset atrial fibrillation, intraventricular conduction defects like RBBBand LBBB were associated with high mortality.

**Key points**

- ECG is non-invasive, low cost, and can be a useful tool to risk stratify COVID-19 pneumonia patients in primary care
- Sinus tachycardia, intraventricular conduction defects like left and right bundle branch block, and new-onset atrial fibrillation predict poor outcome.

**Declaration of patient consent**

The study was approved by institutional ethics committee via letter number - AIIMS/IEC/20/255, dated 09/05/2020 and Clinical Trial Registry of India via letter number CTRI/2020/05/025216[Registered on : 16/05/2020]

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Angeli F, Spanevello A, De Ponti R, Visca D, Marazzato J, Palmiotto G, et al. Electrocardiographic features of patients with COVID-19 pneumonia. Eur J Intern Med 2020;78:101-6.
2. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol 2020;17:259-60.
3. Akhmerov A, Marbán E. COVID-19 and the heart. Circ Res 2020;126:1443-55.
4. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and cardiovascular disease. Circulation 2020;141:1648-55.
5. Rautaharju PM, Surawicz B, Gettes LS, Bailey JJ, Childers R, Deal BJ, et al. AHA/AACC/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part IV: The ST segment, T and U waves, and the QT interval: 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. Circulation 2009;119:e241-50.
6. Wagner GS, Macfarlane P, Wells H, Josephson M, Gorgels A, Mirvis DM, et al. AHA/AACC/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part VI: Acute ischemia/infarction: 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 2009;53:1003-11.
7. Surawicz B, Knilans T. Chou’s Electrocardiography in Clinical Practice. 5th ed. Philadelphia, PA: WB Saunders; 2001.
8. Stone E, Kiat H, McLachlan CS. Atrial fibrillation in COVID-19: A review of possible mechanisms. FASEB J 2020;34:11347-54.
9. Colon CM, Barrios JG, Chiles JW, McElwee SK, Russell DW, Maddox WR, et al. Atrial arrhythmias in COVID19 patients. ACC Clin Electrophysiol 2020;6:1189-90.
10. Kuipers S, Kloouwenberg PMK, Cremer OL. Incidence, risk factors and outcomes of new-onset atrial fibrillation in patients with sepsis: A systematic review. Crit Care 2014;18:698.
11. Goodman S, Weiss Y, Weissman C. Update on cardiac arrhythmias in the ICU. Curr Opin Crit Care 2008;14:549-54.
12. Aviles RJ, Martin DO, Apperson-Hansen C, Houghtaling PL, Rautaharju P, Kronmal RA, et al. Inflammation as a risk factor for atrial fibrillation. Circulation 2003;108:3006-10.
13. Seguin P, Launey Y. Atrial fibrillation is not just an artefact in the ICU. Crit Care 2010;14:182.
14. Walkey AJ, Wiener RS, Ghobrial JM, Curtis LH, Benjamin EJ. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. JAMA 2011;306:2248-54.
15. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:802-10.
16. Aulin J, Siegbahn A, Hijazi Z, Ezekowitz MD, Andersson U, Connolly SJ, et al. Interleukin-6 and C-reactive protein and risk for death and cardiovascular events in patients with atrial fibrillation. Am Heart J 2015;170:1151-60.
17. Amdur RL, Mukherjee M, Go A, Barrows IR, Ramezani A, Shoji J, et al. Interleukin-6 is a risk factor for atrial fibrillation in chronic kidney disease: Findings from the CRIC study. PLoS One 2016;11:e0148189.
18. Ali A, Boutjdir M, Aromolaran AS. Cardiolipotoxicity, inflammation, and arrhythmias: Role for interleukin-6 molecular mechanisms. Front Physiol 2019;9:1866.
19. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, et al. The variety of cardiovascular presentations of COVID-19. Circulation 2020;141:1930-6.
20. Leibovici L, Gafter-Gvili A, Paul M, Almanasreh N, Tacconelli E, Andreassen S, et al. Relative tachycardia in patients with sepsis: An independent risk factor for mortality. QJM 2007;100:629-34.
21. Otake H, Suzuki H, Honda T, Maruyama Y. Influences of autonomic nervous system on atrial arrhythmogenic substrates and the incidence of atrial fibrillation in diabetic heart. Int Heart J 2009;50:627-41.
22. Bers DM. Cardiac excitation-contraction coupling. Nature 2002;415:198-205.
23. Keurs HET, Boyden PA. Calcium and arrhythmogenesis. Physiol Rev 2007;87:457-506.
24. McCullough SA, Goyal P, Krishnan U, Choi JJ, Safford MM, Okin PM. Electrocardiographic findings in coronavirus disease-19: Insights on mortality and underlying myocardial processes. J Card Fail 2020;26:626-32.
25. Wang Y, Chen L, Wang J, He X, Huang F, Chen J, et al. Electrocardiogram analysis of patients with different types of COVID-19. Ann Noninvasive Electrocardiol 2020;25:e12806.
26. Long B, Brady WJ, Bridwell RE, Ramzy M, Montrief T, Singh M, et al. Electrocardiographic manifestations of COVID-19. Am J Emerg Med 2021;41:96-103.